Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
RABOTIDE FAST

2. Qualitative and quantitative composition
Each uncoated tablet contains Rabeprazole Sodium USP 20 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Tablets
Reddish brown coloured, oval shaped biconvex uncoated tablet, plain on both sides and Alu-Alu blister packed.

4. Clinical particulars
4.1 Therapeutic indications
Healing of erosive or ulcerative gastroesophageal reflux disease (GERD)
Rabeprazole is indicated for short-term (4 to 8 weeks) treatment in the healing and symptomatic relief of erosive or ulcerative gastroesophageal reflux disease (GERD). For those patients who have not healed after 8 weeks of treatment, an additional 8-week course of rabeprazole may be considered.

Maintenance of healing of erosive or ulcerative gastroesophageal reflux disease (GERD)
Rabeprazole is indicated for maintaining healing and reduction in relapse rates of heartburn symptoms in patients with erosive or ulcerative gastroesophageal reflux disease (GERD Maintenance). Controlled studies do not extend beyond 12 months.

Treatment of symptomatic gastroesophageal reflux disease (GERD)
Rabeprazole is indicated for the treatment of daytime and nighttime heartburn and other symptoms associated with GERD.

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

Helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence Rabeprazole in combination with amoxicillin and clarithromycin 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.

Treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome

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

4.2 Posology and method of administration

Healing of erosive or ulcerative gastroesophageal reflux disease (GERD)
The recommended adult oral dose is one Rabezole FR 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 Rabeprazole may be considered.

Maintenance of healing of erosive or ulcerative gastroesophageal reflux disease (GERD Maintenance)
The recommended adult oral dose is one Rabezole FR to be taken once daily.

Treatment of symptomatic gastroesophageal reflux disease (GERD)
The recommended adult oral dose is one Rabezole FR to be taken once daily for 4 weeks. If symptoms do not resolve completely after 4 weeks, an additional course of treatment may be considered.

Healing of duodenal ulcers
The recommended adult oral dose is one Rabezole FR 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.

Treatment of pathological hypersecretory conditions including Zollinger-Ellison Syndrome.
The dosage of rabeprazole 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 patient needs and should continue for as long as clinically indicated. Some patients may require divided doses. Doses up to 100 mg QD and 60 mg BID have been administered. Some patients with Zollinger-Ellison syndrome have been treated continuously with rabeprazole for up to one year.
No dosage adjustment is 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.
The route of administration is oral

4.3 Contraindications

Rabeprazole is contraindicated in patients with known hypersensitivity to Rabeprazole, substituted benzimidazoles or to any component of the formulation.

4.4 Special warnings and precautions for use

Precautions:

General

Symptomatic response to therapy with Rabeprazole does not preclude the presence of gastric malignancy. More number of patients with healed GERD who were treated for up to 40 months with Rabeprazole had atrophy of glands in the gastric body as compared to baseline. Approximately 4% of patients had intestinal metaplasia at some point during follow-up, but no consistent changes were seen.

No evidence of significant drug related safety problems was seen in a study of patients with mild to moderate hepatic impairment. However because there are no clinical data on the use of rabeprazole in the treatment of patients with severe hepatic dysfunction, caution is advised when treatment with Rabeprazole is first initiated in such patients.

Effect on ability to drive and use machines: Based on the pharmacodynamic properties and the adverse events profile, it is unlikely that Rabeprazole would cause an impairment of driving performance or compromise the ability to use machinery. If however, alertness is impaired due to somnolence, it is recommended that driving and operating complex machinery be avoided.

Warning

Since each tablet of Rabezole FR contains 10.3 mEq sodium, those on severe salt restricted diet or requiring curtailing excess sodium intake, should accordingly adjust their dietary intake

4.5 Interaction with other medicinal products and other forms of interaction

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 dose, 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. There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including rabeprazole, and warfarin concomitantly. Increase 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 increase in INR and prothrombin time.

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.

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 increase 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.

4.6 Pregnancy and Lactation

There are no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
It is not known if unmetabolized rabeprazole is excreted in human breast milk. 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.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamic properties and the adverse events profile, it is unlikely that rabeprazole would cause an impairment of driving performance or compromise the ability to use machinery. If however, alertness is impaired due to somnolence, it is recommended that driving and operating complex machinery be avoided.

4.8 Undesirable effects

Adverse effects with Rabeprazole are mild to moderate in intensity and include malaise, diarrhea, nausea, skin eruptions, headache and dizziness.
Abnormal laboratory findings (increased hepatic enzymes, LDH, blood urea nitrogen) observed with Rabeprazole were similar in incidence and severity with comparator agents and reversible with cessation of therapy.
Inform your doctor in case of any adverse reactions related to drug use.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via National Pharmacovigilance Electronic Reporting Systems' to the respective National Regulatory Authorities.

4.9 Overdose

There has been no experience with large overdoses with Rabeprazole. Seven reports of accidental overdosage with Rabeprazole have been received. The maximum reported overdose was 80 mg. There were no clinical signs or symptoms associated with any reported overdose. 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. Single oral dose of Rabeprazole at 786 mg/kg and 1024 mg/kg were lethal to mice and rats, respectively. The single oral dose of 2000 mg/kg was not lethal to dogs. The major symptoms of acute toxicity were hypoactivity, labored respiration, lateral or prone position and convulsion in mice and rats and watery diarrhea, tremor, convulsion and coma in dogs.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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 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, 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. 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.

Rabeprazole can suppress gastric Helicobacter pylori in patients with duodenal ulcer and/or reflux oesophagitis infected with the organism, probably via the binding to the bacteria and resultant inhibition of urease activity.

Antisecretory activity

Rabezole FR neutralizes the acid in the stomach immediately within few minutes. This results in faster relief from hyperacidity symptoms as compared to conventional rabeprazole whose onset of action may even take 2 hours.

The median inhibitory effect of rabeprazole on 24 hour gastric acidity is 88% of maximal after the first dose. Rabeprazole 20 mg inhibits basal and peptone meal-stimulated acid secretion versus placebo by 86% and 95%, respectively, and increases the percent of a 24-hour period that the gastric pH >3 from 10% to 65%. This relatively prolonged pharmacodynamic action compared to the short pharmacokinetic half-life (1-2 hours) reflects the sustained inactivation of the H+, K+ ATPase.

Effects on esophageal acid exposure

In patients with gastroesophageal reflux disease (GERD) and moderate to severe esophageal acid exposure, rabeprazole decreased 24-hour esophageal acid exposure. Normalization of 24-hour intraesophageal acid exposure was correlated to gastric pH>4 for at least 35% of the 24-hour period; this level was achieved in 90% of subjects receiving Rabezole FR.

Effects on serum gastrin

In patients given daily doses of rabeprazole for up to eight weeks to treat ulcerative or erosive esophagitis and in patients treated for up to 52

weeks to prevent recurrence of disease the median fasting gastrin level increased in a dose-related manner. In a group of subjects treated daily with rabeprazole 20 mg for 4 weeks a doubling of mean serum gastrin concentrations were observed. Approximately 35% of these treated subjects developed serum gastrin concentrations above the upper limit of normal.

Effects on Enterochromaffin-like (ECL) Cells

Increased serum gastrin secondary to antisecretory agents stimulates proliferation of gastric ECl cells which, over time, may result in ECl cell hyperplasia in rats and mice and gastric carcinoids in rats, especially in females. In over 400 patients treated with rabeprazole (10 or 20 mg/day) for up to one year, the incidence of ECl cell hyperplasia increased with time and dose. However, no patient developed the adenomatoid, dysplastic or neoplastic changes of ECl cells in the gastric mucosa. No patient developed the carcinoid tumors observed in rats.

Endocrine effects

Studies in humans for up to one year have not revealed clinically significant effects on the endocrine system.

Other effects

In humans treated with rabeprazole for up to one year, no systemic effects have been observed on the central nervous, lymphoid, hematopoietic, renal, hepatic, cardiovascular, or respiratory systems. No data are available on long-term treatment with rabeprazole and ocular effects.

5.2 Pharmacokinetic properties

Rabezole FR rapidly disintegrates within the aqueous media of the stomach since it is buffered. The buffering of rabeprazole ensures that disintegration occurs even with minimal stomach motility.

Absorption: After oral administration of Rabezole FR, peak plasma concentrations (Cmax) of Rabeprazole occur promptly over a period of 0.5 hour (Tmax). The Cmax and area under the curve (AUC) are attained with Rabezole FR are significantly higher as compared with conventional Rabeprazole. There is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 hours; the pharmacokinetics of Rabeprazole are not altered by multiple dosing. The plasma half life ranges from 1 to 2 hours.

Distribution: Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism: Rabeprazole is extensively metabolized in the liver primarily by cytochromes P450 3A (CYP3A) to a sulphone metabolite and cytochrome P450 2C19 (CYP2CI9) to desmethyl rabeprazole. The thioether and sulphone metabolites were not observed to have significant antisecretory activity.

Elimination : Following a single 20 mg oral dose of Rabeprazole, approximately 90% of the drug is eliminated in the urine, primarily as thioether carboxylic acid; its glucuronide, and mercapturic acid

metabolites. The remainder of the dose is recovered in the feces. No unchanged rabeprazole was recovered in the urine or feces.
Special Populations
Geriatric: There is no evidence of drug accumulation after once daily administration. Pediatric: The pharmacokinetics of rabeprazole in pediatric patients under the age of 18 years has not been studied.
Gender and Race: In analyses adjusted for body mass and height, Rabeprazole pharmacokinetics showed no clinically significant differences between male and female subjects.
No information exists on Rabeprazole disposition in patients with severe hepatic impairment.

5.3 Preclinical safety data

Rabeprazole: Non-clinical effects were observed only at exposures sufficiently in excess of the maximum human exposure that make concerns for human safety negligible in respect of animal data. Studies on mutagenicity gave equivocal results. Tests in mouse lymphoma cell line were positive, but in vivo micronucleus and in vivo and in vitro DNA repair tests were negative. Carcinogenicity studies revealed no special hazard for humans.

6. Pharmaceutical Particulars

6.1 List of Excipients

Calcium carbonate BP/Ph Eur
Light Magnesium Oxide BP/Ph Eur
CrospovidoneBP/Ph Eur
Povidone K 90 BP/Ph Eur
Ferric Oxide Red USP-NF
Sodium Bicarbonate BP/Ph Eur
Magnesium Stearate BP/Ph Eur

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

24 months

6.4 Special Precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and Content of container

Alu -Alu Blister of 10 Tablets. Box containing 100 tablets

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing Authorization Holder

Inventia Healthcare Limited
F1-F1/1, Additional Ambernath M.I.D.C., Ambernath (East) - 421 506,

Dist. Thane, INDIA.

8. Marketing Authorization Number
H2022/CTD8390/16473

9. Date of first authorization/renewal of the authorization
2023 November 22

10. Date of revision of the text
2023 November 22