Summary of Product Characteristics

1. Name of the medicinal product

Omega Rapid Dry Suspension

2. Qualitative and quantitative composition

Each Sachet Contains:
Omeprazole ……. 20 mg
Sodium Bicarbonate……. 1680 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

White colored granules Mix powder

4. Clinical particulars

4.1 Therapeutic indications

OMEGA RAPID (Omeprazole + Sodium bicarbonate) powder for oral suspension is indicated in adults for the:

- For the treatment of Gastroesophageal Reflux Disease (GERD)
  - Treatment of heartburn and other symptoms associated with GERD for up to 4 weeks.
  - Short-term treatment (4 to 8 weeks) of EE due to acid-mediated GERD which has been diagnosed by endoscopy in adults.
- Short-term treatment of active duodenal ulcer. Most patients heal within four weeks. Some patients may require an additional four weeks of therapy.
- Short-term treatment (4 to 8 weeks) of active benign gastric ulcer.
- For m*aintenance treatment of healing of erosive esophagitis* due to acid-mediated GERD.
- For reduction of risk of upper gastrointestinal bleeding in critically Ill patients (40mg oral suspension only)

4.2 Posology and method of administration

OMEGA RAPID (Omeprazole + Sodium bicarbonate) powder for oral suspension should be administered as per recommended dosing given in below table. Only 40mg OMEGA RAPID for oral suspension is indicated for the reduction of risk of upper GI bleeding in critically ill adult patients and the dosage regimen is summarized in below table. All recommended dosages are based upon omeprazole content.

Recommended doses for Adults (18 years & older)

Indication	Recommended Dose	Treatment Duration
Treatment of Active Duodenal Ulcer	20 mg once daily	4 weeks[1,2]
Treatment of Active Benign Gastric Ulcer	40 mg once daily	4 to 8 weeks
Treatment of Symptomatic GERD	20 mg once daily	Up to 4 weeks

Treatment of EE due to Acid-Mediated GERD	20 mg once daily	4 to 8 weeks[2]
Maintenance of Healing of EE due to Acid-Mediated GERD	20 mg once daily	Controlled studies do not extend beyond 12 months.
Reduction of Risk of Upper GI Bleeding in Critically Ill Patients	40 mg initially; followed by 40 mg 6 to 8 hours later; and 40 mg once daily thereafter	14 days
[1] Most patients heal within 4 weeks. Some patients may require an additional 4 weeks of therapy. [2] The efficacy of Omeprazole + Sodium bicarbonate powder for oral suspension used for longer than 8 weeks in patients with EE has not been established. If a patient does not respond to 8 weeks of treatment, an additional 4 weeks of treatment may be given. If there is recurrence of EE or GERD symptoms (e.g., heartburn), additional 4 to 8 week courses of OMEGA RAPID (Omeprazole + Sodium bicarbonate) may be considered.		

Since both 20mg and 40mg oral suspension sachets contain the same amount of sodium bicarbonate (1680mg), two sachets of OMEGA RAPID (Omeprazole + Sodium bicarbonate) 20mg are not equivalent to one sachet of OMEGA RAPID (Omeprazole + Sodium bicarbonate) 40mg; therefore two 20mg sachets of OMEGA RAPID (Omeprazole + Sodium bicarbonate) should not be substituted for one sachet OMEGA RAPID (Omeprazole + Sodium bicarbonate) 40mg.

Special populations

Pregnancy:

There are no adequate and well-controlled studies on the use of omeprazole in pregnant women. Omeprazole should be used during pregnancy only if the potential benefit to pregnant women justifies the potential risk to the fetus.

Lactation:

Omeprazole is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from omeprazole; a decision should be made whether, to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. In addition, sodium bicarbonate should be used with caution in nursing mothers.

Pediatric Use:

Safety and effectiveness have not been established in pediatric patients.

Geriatric Use:

No differences in safety and effectiveness between the elderly and younger subjects were found. Other reported clinical experience has not identified differences in response between the elderly and younger subjects, but greater sensitivity of some older individuals cannot be ruled out. No dosage adjustment is necessary in the elderly.

Hepatic Impairment:

Avoid use of ***OMEGA RAPID (Omeprazole + Sodium bicarbonate)*** in patients with hepatic impairment for maintenance of healing of erosive esophagitis.

Method of administration

OMEGA RAPID (Omeprazole + Sodium bicarbonate) for oral suspension is intended to be mixed with water and administered orally or via a nasogastric (NG) or orogastric (OG) tube. If administered orally, take on an empty stomach at least one hour before a meal. If administered via NG or OG tube, suspend enteral feeding approximately 3 hours before and 1 hour after administration of OMEGA RAPID (Omeprazole + Sodium bicarbonate) for oral suspension.

Oral Administration: Empty the contents of a packet into a small cup containing 1–2 tablespoon of water. Do not use other liquids or foods. Stir well and drink immediately. Refill cup with water and drink immediately.

Nasogastric (NG) or Orogastric (OG) Tube Administration: Add 20 mL of water to a catheter tipped syringe and then add the contents of a packet. Use an appropriately-sized catheter tipped syringe. Do not mix with liquids or foods other than water. Shake the syringe to dissolve the powder. Administer through the NG or orogastric tube into the stomach right away. Refill the syringe with an equal amount of water. Shake and flush any remaining contents from the NG tube or orogastric tube into the stomach.

4.3 Contraindications

- Hypersensitivity to any component of the formulation.
- In patients receiving rilpivirine containing products.

4.4 Special warnings and precautions for use

Gastric Malignancy: In adults, symptomatic response does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing.

Acute Interstitial Nephritis: *Observed in patients taking PPIs. Discontinue* OMEGA RAPID (Omeprazole + Sodium bicarbonate) *if acute interstitial nephritis develops.*

Sodium Bicarbonate Buffer Content: *Take sodium content into consideration in patients on a sodium-restricted diet or those at risk for developing congestive heart failure. Avoid in patients with Bartter's syndrome, hypokalemia, hypocalcemia, and problems with acid-base balance. Chronic administration of bicarbonate with calcium or milk can cause milk-alkali syndrome. Chronic use of sodium bicarbonate may lead to systemic alkalosis, and increased sodium intake can produce edema and weight gain.*

Clostridium difficile-Associated Diarrhea: *PPI therapy may be associated with increased risk. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.*

Bone Fracture: *Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.*

Cutaneous and Systemic Lupus Erythematosus: Mostly cutaneous; new onset or exacerbation of existing disease; discontinue OMEGA RAPID (Omeprazole + Sodium bicarbonate) *and refer to specialist for evaluation.*

Cyanocobalamin (Vitamin B-12) Deficiency: *Daily treatment with any acid-suppressing medications*

over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B-12) caused by hypo-or achlorhydria.

Hypomagnesemia: *Reported rarely with prolonged treatment with PPIs for at least three months, in most cases after a year of therapy. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.*

Fundic Gland Polyps: *Risk increases with long-term use, especially beyond one year. Use the shortest duration of therapy.*

4.5 Interaction with other medicinal products and other forms of interaction

Antiretrovirals:

Decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir and nelfinavir) when used concomitantly with omeprazole may reduce antiviral effect and promote the development of drug resistance. Avoid concomitant use with *OMEGA RAPID (Omeprazole + Sodium bicarbonate).*

Warfarin:

Increased INR and prothrombin time in patients receiving omeprazole, and warfarin concomitantly. Monitor INR and prothrombin time and adjust the dose of warfarin, if needed, to maintain target INR range.

Methotrexate:

Concomitant use of omeprazole with methotrexate (primarily at high dose) may elevate and prolong serum concentrations of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities. A temporary withdrawal of *OMEGA RAPID (Omeprazole + Sodium bicarbonate)* may be considered in some patients receiving high-dose methotrexate.

CYP2C19 Substrates (e.g., clopidogrel, citalopram, cilostazol, phenytoin, diazepam)

***Clopidogrel*:**

Concomitant use of omeprazole 80 mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant use with *OMEGA RAPID (Omeprazole + Sodium bicarbonate)*. Consider use of alternative anti-platelet therapy.

Citalopram:

Increased exposure of citalopram leading to an increased risk of QT prolongation. Limit the dose of citalopram to a maximum of 20 mg per day.

Cilostazol:

Increased exposure of one of the active metabolites of cilostazol (3,4-dihydrocilostazol). Reduce the dose of cilostazol to 50 mg twice daily.

Phenytoin:

Potential for increased exposure of phenytoin. Monitor phenytoin serum concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.

Diazepam:

Increased exposure of diazepam. Monitor patients for increased sedation and reduce the dose of diazepam as needed.

Digoxin:

Potential for increased exposure of digoxin. Monitor digoxin concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.

Drugs Dependent on Gastric pH for Absorption (e.g., iron salts, erlotinib, dasatinib, nilotinib, mycophenolate mofetil, ketoconazole/itraconazole):

Omeprazole can reduce the absorption of other drugs due to its effect on reducing intragastric acidity. Use OMEGA RAPID (Omeprazole + Sodium bicarbonate) *with caution in transplant patients receiving MMF (Mycophenolate mofetil).*

Tacrolimus: Potential for increased exposure of tacrolimus, especially in transplant patients. Monitor tacrolimus whole blood concentrations. Dose adjustment may be needed to maintain therapeutic drug concentrations.

Interactions with Investigations for Neuroendocrine Tumors:

Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. Providers should temporarily stop *OMEGA RAPID (Omeprazole + Sodium bicarbonate)* treatment for at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high.

Interaction with Secretin Stimulation Test:

Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma. Temporarily stop *OMEGA RAPID (Omeprazole + Sodium bicarbonate)* treatment at least 14 days before assessing to allow gastrin levels to return to baseline.

False Positive Urine Tests for THC:

There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving PPIs. An alternative confirmatory method should be considered to verify positive results.

CYP2C19 or CYP3A4 Inducers:

Decreased exposure of omeprazole when used concomitantly with strong inducers. Avoid concomitant use with OMEGA RAPID (Omeprazole + Sodium bicarbonate).

CYP2C19 or CYP3A4 Inhibitors: Increased exposure of omeprazole.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies on the use of OMEGA RAPID in pregnant women. Available epidemiologic data fail to demonstrate an increased risk of major congenital malformations or other adverse pregnancy outcomes with first trimester omeprazole use. Teratogenicity was not observed in animal reproduction studies with administration of oral esomeprazole magnesium in rats and rabbits with doses about68 times and 42 times, respectively, an oral human dose of 40 mg (based on a body surface area basis for a 60 kg person). However, changes in bone morphology were observed in offspring of rats dosed through most of pregnancy and lactation at doses equal to or greater than

approximately 33.6 times an oral human dose of 40 mg (see Animal Data). Because of the observed effect at high doses of esomeprazole magnesium on developing bone in rat studies, OMEGA RAPID should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breast-feeding

Omeprazole concentrations have been measured in breast milk of a woman following oral administration of 20 mg. The peak concentration of omeprazole in breast milk was less than 7% of the peak serum concentration. The concentration will correspond to 0.004 mg of omeprazole in 200 mL of milk. Because omeprazole is excreted in human milk, because of the potential for serious adverse reactions in nursing infants from omeprazole, and because of the potential for tumorigenicity shown for omeprazole in rat carcinogenicity studies, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. In addition, sodium bicarbonate should be used with caution in nursing mothers.

Pediatric Use

Safety and effectiveness of OMEGA RAPID have not been established in pediatric patients less than 18 years of age. Juvenile Animal Data In a juvenile rat toxicity study, esomeprazole was administered with both magnesium and strontium salts at oral doses about 34 to 68 times a daily human dose of 40 mg on a body surface area basis. Increases in death were seen at the high dose, and at all doses of esomeprazole, there were decreases in body weight, body weight gain, femur weight and femur length, and decreases in overall growth

4.7 Effects on ability to drive and use machines

Certain undesirable effects (e.g. dizziness / vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

4.8 Undesirable effects

Following adverse reactions have been reported in patients:

Omeprazole

Body as a Whole: Hypersensitivity reactions, including anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, urticaria, fever, pain, fatigue, malaise, and systemic lupus erythematosus.

Cardiovascular: Chest pain or angina, tachycardia, bradycardia, palpitation, elevated blood pressure, and peripheral edema.

Gastrointestinal: Pancreatitis (some fatal), anorexia, irritable colon, flatulence, fecal discoloration, esophageal candidiasis, mucosal atrophy of the tongue, dry mouth, stomatitis, abdominal swelling and fundic gland polyps. Gastroduodenal carcinoids have been reported in patients with Zollinger-Ellison syndrome on long-term treatment with omeprazole.

Hepatic: Mild and, rarely, marked elevations of liver function tests [ALT (SGPT), AST (SGOT), γ-glutamyl transpeptidase, alkaline phosphatase, and bilirubin (jaundice)]. In rare instances, overt liver disease has occurred, including hepatocellular, cholestatic, or mixed hepatitis, liver necrosis (some fatal), hepatic failure (some fatal), and hepatic encephalopathy.

Infections and Infestations: Clostridium difficile-associated diarrhea.

Metabolism and Nutritional Disorders: Hyponatremia, hypoglycemia, hypomagnesemia, and weight gain.

Musculoskeletal: Muscle cramps, myalgia, muscle weakness, joint pain, bone fracture, and leg pain.

Nervous System/Psychiatric: Psychic disturbances including depression, agitation, aggression, hallucinations, confusion, insomnia, nervousness, tremors, apathy, somnolence, anxiety, dream abnormalities; vertigo; paresthesia; and hemifacial dysesthesia.

Respiratory: Epistaxis, pharyngeal pain.

Skin: Severe generalized skin reactions including toxic epidermal necrolysis (TEN; some fatal), Stevens-Johnson syndrome, cutaneous lupus erythematosus and erythema multiforme (some severe); purpura and/or petechiae (some with

rechallenge); skin inflammation, urticaria, angioedema, pruritus, photosensitivity, alopecia, dry skin, and hyperhidrosis.

Special Senses: Tinnitus, taste perversion.

Ocular: Blurred vision, ocular irritation, dry eye syndrome, optic atrophy, anterior ischemic optic neuropathy, optic neuritis, and double vision.

Urogenital: Interstitial nephritis (some with positive rechallenge), urinary tract infection, microscopic pyuria, urinary frequency, elevated serum creatinine, proteinuria, hematuria, glycosuria, testicular pain, and gynecomastia.

Hematologic: Rare instances of pancytopenia, agranulocytosis (some fatal), thrombocytopenia, neutropenia, leukopenia, anemia, leukocytosis, and hemolytic anemia have been reported.

Sodium Bicarbonate: metabolic alkalosis, seizures, and tetany.

4.9 Overdose

Omeprazole: Doses ranged up to 2400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, vomiting, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in clinical experience with the recommended dosage. No specific antidote for omeprazole overdosage is known. Omeprazole is extensively protein bound and is, therefore, not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

Sodium Bicarbonate: Overdosage of sodium bicarbonate can cause electrolyte abnormalities (hypocalcemia, hypokalemia, hypernatremia), metabolic alkalosis, and seizures. Institute supportive care and correct electrolyte abnormalities.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Combination of Proton Pump Inhibitor and Antacid

ATC code: A02BC01

Mechanism of action

Omeprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonistic properties, but that suppress gastric acid secretion by specific inhibition of the H+/K+ ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after rapid disappearance from plasma, omeprazole can be found within the gastric mucosa for a day or more.

Omeprazole is acid labile and thus rapidly degraded by gastric acid. OMEGA RAPID Capsules and Powder for Oral Suspension are immediate-release formulations that contain sodium bicarbonate which raises the gastric pH and thus protects omeprazole from acid degradation.

Pharmacodynamics:

Antisecretory Activity:

Results from a pharmacokinetic/pharmacodynamic (PK/PD) study of the antisecretory effect of repeated once-daily dosing of 40 mg and 20 mg of OMEGA RAPID for oral suspension in healthy subjects are shown in below;

	Once-Daily Dosage of ZEGERID for Oral Suspension	
Parameter	**40 mg omeprazole and 1,680 mg sodium bicarbonate (n = 24)**	**20 mg omeprazole and 1,680 mg sodium bicarbonate (n = 28)**
% Decrease from Baseline for Integrated Gastric Acidity (mmol•hr/L)	84%	82%
Coefficient of Variation	20%	24%
% Time Gastric pH > 4* (Hours)*	77% (18.6 h)	51% (12.2 h)
Coefficient of Variation	27%	43%
Median pH	5.2	4.2
Coefficient of Variation	17%	37%
Note: Values represent medians. All parameters were measured over a 24-hour period.		

* P < 0.05 20 mg vs. 40 mg

Enterochromaffin-like (ECL) Cell Effects:

Human gastric biopsy specimens have been obtained from more than 3000 patients treated with omeprazole in long-term clinical trials. The incidence of ECL cell hyperplasia in these studies increased with time; however, no case of ECL cell carcinoids, dysplasia, or neoplasia has been found in these patients. These studies are of insufficient duration and size to rule out the possible influence of long-term administration of omeprazole the development of any premalignant or malignant conditions.

Serum Gastrin Effects In studies involving more than 200 patients, serum gastrin levels increased during the first 1 to 2 weeks of once-daily administration of therapeutic doses of omeprazole in parallel with inhibition of acid secretion. No further increase in serum gastrin occurred with continued treatment. In comparison with histamine H -receptor antagonists, the median increases produced by 20 mg doses of omeprazole were higher (1.3 to 3.6-fold vs. 1.1- to 1.8-fold increase). Gastrin values returned to

pretreatment levels, usually within 1 to 2 weeks after discontinuation of therapy. Increased gastrin causes enterochromaffin-like cell hyperplasia and increased serum Chromogranin A (CgA) levels. The increased CgA levels may cause false positive results in diagnostic investigations for neuroendocrine tumors

Other Effects:

Systemic effects of omeprazole in the central nervous system (CNS), cardiovascular and respiratory systems have not been found to date.

5.2 Pharmacokinetic properties

Absorption

If omeprazole is administered on an empty stomach 1 hour prior to a meal, the absorption of omeprazole is rapid, with mean peak plasma levels (% CV) of omeprazole being 1954 ng/mL (33%) and 1526 ng/mL (49%) respectively and time to peak of approximately 30 minutes (range 10-90 min) after a single-dose or repeated- dose administration.

Following single or repeated once daily dosing, peak plasma concentrations of omeprazole are approximately proportional from 20 to 40 mg doses, but a greater than linear mean AUC (three-fold increase) is observed when doubling the dose to 40 mg. The bioavailability of omeprazole increases upon repeated administration. When powder for oral suspension is administered 1 hour after a meal, the omeprazole AUC is reduced by approximately 24% relative to administration 1 hour prior to a meal.

Distribution

Omeprazole is bound to plasma proteins. Protein binding is approximately 95%.

Elimination

Following absorption, omeprazole is almost completely metabolized in the liver, primarily by the cytochrome P450 isoenzyme CYP2C19 to form hydroxy-omeprazole and to a small extent by CYP3A4 to form omeprazole sulfone. These metabolites are inactive and excreted mostly in the urine and to a lesser extent in the bile. The majority of the dose (77%) was eliminated in the urine. The remainder of the dose was recoverable in the feces. The mean plasma omeprazole half-life is approximately 1 hour (ranging from 0.4 to 3.2 hours) and the total body clearance is 500-600mL/min.

Special populations

Geriatric Patients:

The elimination rate was somewhat decreased in the elderly and bioavailability was increased. Omeprazole was 76% bioavailable when a single 40mg oral dose of omeprazole (buffered solution) was administered to healthy elderly subjects, versus 58% in young subjects given the same dose. The plasma clearance of omeprazole was 250mL/min (about half that of young subjects) and its plasma half-life averaged one hour, similar to that of young healthy subjects.

Pediatric:

The pharmacokinetics of omeprazole has not been studied in patients <18 years of age.

Gender:

There are no known differences in the absorption or excretion of omeprazole between males and females.

Asian population:

In pharmacokinetic studies of single 20-mg omeprazole doses, an increase in AUC of approximately four-fold was noted in Asian subjects compared to Caucasians. Dose adjustment, particularly where maintenance of healing of erosive esophagitis is indicated, for Asian subjects should be considered.

Patients with Hepatic Impairment:

In patients with chronic hepatic disease, the bioavailability of omeprazole increased to approximately 100% compared to healthy subjects, reflecting decreased first-pass effect, and the plasma half-life of the drug increased to nearly 3 hours compared to the in healthy subjects of 0.5 to 1 hour. Plasma clearance averaged 70 mL/min, compared to a value of 500 to 600 mL/min in healthy subjects.

Patients with Renal Impairment:

In patients with chronic renal impairment (creatinine clearance between 10 and 62 mL/min/1.73 m^2), the disposition of omeprazole was very similar to that in healthy subjects, although there was a slight increase in bioavailability. Because urinary excretion is a primary route of excretion of omeprazole metabolites, their elimination slowed in proportion to the decreased creatinine clearance.

5.3 Preclinical safety data

Carcinogenesis, Mutagenesis, Impairment of Fertility;

In two 24-month carcinogenicity studies in rats, omeprazole at daily doses of 1.7, 3.4, 13.8, 44 and 140.8 mg/kg/day (approximately 0.4 to 34.2 times the human dose of 40 mg/day on a body surface area basis) produced gastric ECL cell carcinoids in a doserelated manner in both male and female rats; the incidence of this effect was markedly higher in female rats, which had higher blood levels of omeprazole. Gastric carcinoids seldom occur in the untreated rat. In addition, ECL cell hyperplasia was present in all treated groups of both sexes. In one of these studies, female rats were treated with 13.8 mg omeprazole/kg/day (approximately 3.36 times the human dose of 40 mg/day on a body surface area basis) for one year, then followed for an additional year without the drug. No carcinoids were seen in these rats. An increased incidence of treatment-related ECL cell hyperplasia was observed at the end of one year (94% treated versus 10% controls). By the second year the difference between treated and control rats was much smaller (46% versus 26%) but still showed more hyperplasia in the treated group. Gastric adenocarcinoma was seen in one rat (2%). No similar tumor was seen in male or female rats treated for two years. For this strain of rat no similar tumor has been noted historically, but a finding involving only one tumor is difficult to interpret. In a 52-week toxicity study in Sprague Dawley rats, brain astrocytomas were found in a small number of males that received omeprazole at dose levels of 0.4, 2, and 16 mg/kg/day (about 0.1 to 3.9 times the human dose of 40 mg/day on a body surface area basis). No astrocytomas were observed in female rats in this study. In a 2-year carcinogenicity study in Sprague Dawley rats, no astrocytomas were found in males and females at the high dose of 140.8 mg/kg/day (about 34 times the human dose of 40 mg/day on a body surface area basis). A 78-week mouse carcinogenicity study of omeprazole did not show increased tumor occurrence, but the study was not conclusive. A 26-week p53 (+/-) transgenic mouse carcinogenicity study was not positive.

Omeprazole was positive for clastogenic effects in an in vitro human lymphocyte chromosomal aberration assay, in one of two in vivo mouse micronucleus tests, and in an in vivo bone marrow cell chromosomal aberration assay. Omeprazole was negative in the in vitro Ames test, an in vitro mouse lymphoma cell forward mutation assay and an in vivo rat liver DNA damage assay.

In a 24-month carcinogenicity studies in rats, a dose-related significant increase in gastric carcinoid tumors and ECL cell hyperplasia was observed in both male and female animals. Carcinoid tumors have also been observed in rats subjected to fundectomy or long-term treatment with other PPIs or high doses of H -receptor antagonists.

Omeprazole at oral doses up to 138 mg/kg/day (about 33.6 times the human dose of 40 mg/day on a body surface area basis) was found to have no effect on the fertility and general reproductive performance in rats.

6. Pharmaceutical particulars

6.1 List of excipients

- Sucralose
- Peppermint Durarome Flavor
- Mannitol
- Xanthan Gum

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Do not store above 30 ° C

6.5 Nature and contents of container

1x10's (Sachet Pack)

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Name of Applicant: Ferozsons Laboratories Limited
Head office Address: 5-Km Sunder Raiwind Road, Raiwind Lahore, Pakistan
Website: www.ferozsons-labs.com
Tel: +92-42-36026700
Fax: +92-42-36026701
Email: info@ferozsons-labs.com

8. Marketing authorization number(s)

H2019/CTD4778/821ER

9. Date of first authorization:

26/07/2026

10. Date of revision of the text

26/07/2026