Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

PRAZIM 20 (Gastro resistant Omeprazole Capsules BP 20mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains:
Omeprazole BP 20 mg
(As enteric coated pellets)

See section 6.1 for a complete list of excipients.

3. PHARMACEUTICAL FORM

Hard gelatine capsules
Pink transparent/ clear transparent, size '2', hard gelatin capsules filled with white to off white enteric coated pellets.

4. CLINICAL CHARACTERISTICS

4.1 Therapeutic indications

Omeprazole capsules are indicated in the following cases:

Adults

- For the treatment of duodenal ulcer
- To prevent relapse of duodenal ulcer
- For the treatment of gastric ulcer
- To prevent the relapse of ulcer ventriculi
- In peptic ulcer disease *combined with an* appropriate antibiotic for the eradication of *Helicobacter pylori (H. pylori).*
- gastric -and duodenal ulcers associated with NSAID use
- when using NSAIDs, to prevent the development of gastric -and duodenal ulcers in patients at risk,
- For the treatment of reflux esophagitis
- Healed for the long-term treatment of reflux esophagitis
- symptomatic gastro- -oesophageal reflux disease
- Zollinger -Ellison syndrome

Children and adolescents
Children older than 1 year and weighing ≥10 kg

- For the treatment of reflux esophagitis.
- For the symptomatic treatment of heartburn and gastric acid regurgitation in gastro-oesophageal reflux disease.

Children and adolescents over 4 years of age

- In combination with antibiotics for the treatment of duodenal ulcers caused by *Helicobacter pylori* infection.

4.2 Dosage and administration

Dosage
Adults
Treatment of duodenal ulcer
For patients with active duodenal ulcer, the recommended dose is 20 mg Omeprazole once daily. Most patients recover within two weeks. In patients who have not fully recovered after the initial treatment, recovery usually occurs during an additional two weeks of therapy. Omeprazole 40 mg once daily is recommended for duodenal ulcer sufferers that are difficult to heal, and recovery is usually achieved within four weeks.

Prevention of duodenal ulcer relapse
To prevent duodenal ulcer relapse in *H. pylori* negative patients or when *H. pylori*

eradication is not possible, the recommended dose is 20 mg Omeprazole once a day. In some patients, once a day 10 mg may be sufficient. In case of ineffective therapy, the dose -can be increased to 40 mg.

Treatment of gastric ulcer
The recommended dose is 20 mg Omeprazole once daily. Most patients recover within four weeks. In patients whose recovery is not complete after the initial treatment, recovery can usually be expected during another four weeks of therapy. Omeprazole 40 mg once daily is recommended for patients with difficult-to-heal stomach ulcers, and healing usually occurs within eight weeks.

Prevention of relapse of ulcer ventriculi
In patients with difficult-to-heal gastric ulcers, the recommended dose for preventing relapse is 20 mg of Omeprazole once a day. If necessary, the dose of Omeprazole -can be increased to 40 mg once a day.

H. pylori eradication in peptic ulcer disease
H. pylori eradication, the selection of the antibiotic should be made depending on the patient's individual drug -tolerance, taking national, regional and local resistant strains into account, and in accordance with the therapeutic guidelines.

- A combination of 20 mg Omeprazole + 500 mg clarithromycin + 1000 mg amoxicillin twice a day for one week or
- 20 mg Omeprazole + 250 mg clarithromycin (or 500 mg) + 400 mg metronidazole (or 500 mg or 500 mg tinidazole) twice daily for one week, or
- 40 mg Omeprazole once a day + -500 mg amoxicillin 3 times a day + 400 mg metronidazole (or 500 mg or 500 mg tinidazole) 3 times a day for one week.

For any treatment regimen, if the patient is still *H.pylori* positive, the treatment can be repeated.

Gastric -and duodenal ulcers associated with NSAID use
In the treatment of gastric and duodenal ulcers associated with NSAID use, the recommended dose is 20 mg Omeprazole once a day. -The vast majority of patients recover within 4 weeks. In patients whose recovery is not complete after the initial treatment, recovery can usually be expected during another four weeks of therapy.

Prevention of stomach and duodenal ulcers in patients at risk when using NSAIDs-
In patients at risk (over 60 years of age, a history of gastric -and duodenal ulcers, or bleeding from the upper part of the gastrointestinal tract), the recommended dose is 20 mg Omeprazole once a day to prevent gastric or duodenal ulcers associated with NSAID use.

Treatment of reflux esophagitis
The recommended dose is 20 mg of Omeprazole once a day. Most patients recover within four weeks. In patients whose recovery is not complete after the initial treatment, recovery can usually be expected during another four weeks of therapy.
Omeprazole 40 mg once daily is recommended for patients with severe esophagitis, and recovery usually occurs within eight weeks.

Long-term treatment of cured reflux esophagitis
The recommended dose for the long-term treatment of cured reflux esophagitis is 10 mg Omeprazole once a day. If necessary, the dose -can be increased to 20-40 mg Omeprazole once a day.

Treatment of symptomatic gastro-oesophageal reflux disease
The recommended dose is 20 mg of Omeprazole per day. Patients -can respond adequately to even 10 mg per day, so consideration of individual dosing is necessary.
If symptom relief is not achieved after four weeks with Omeprazole 20 mg daily, further investigation is recommended.

Zollinger -Ellison syndrome
Zollinger -Ellison syndrome, dosing should be individualized and continued as long as clinically indicated. The recommended starting dose is 60 mg Omeprazole per day. Severe patients who previously did not respond to other treatments were effectively treated, more than 90% of patients received Omeprazole maintenance therapy of 20,120 mg per day. In the case of a daily dosage of more than 80 mg, the daily dose must be divided into two parts.

Children and adolescents

Children older than 1 year and weighing ≥10 kg
Treatment of reflux esophagitis
Symptomatic treatment of heartburn and gastric acid regurgitation in gastro-oesophageal reflux disease

The dosage recommendation is as follows:

Circle	Body mass	Dosage
Age ≥1 year	10 -20 kg	10 mg once a day. If necessary, the dose -can be increased to 20 mg once a
Age ≥2 years	>20 kg	20 mg once a day. If necessary, the dose -can be increased to 40 mg once a

Reflux oesophagitis: Duration of treatment is 4-8 -weeks.

Symptomatic treatment of heartburn and gastric acid regurgitation in gastro-oesophageal reflux disease:
The duration of the treatment is 2 -4 weeks. If it is not possible to achieve symptom relief after 24 weeks, further examination of the patient is necessary.

Children and adolescents over 4 years of age

Treatment of duodenal ulcer caused by H. pylori infection

When selecting the appropriate combination therapy, consideration should be given to official national, regional, and local guidelines for bacterial resistance, duration of therapy (most often 7 days, but sometimes 14 days), and appropriate use of antibacterial agents.

The treatment should be carried out under the supervision of a specialist. The dosage recommendation is as follows:

Body mass	Dosage
15 -30 kg	Combined with two antibiotics: Omeprazole 10 mg, amoxicillin 25 mg/kg body weight, and clarithromycin 7.5 mg/kg body weight together, twice daily for one week
31 -40 kg	Combined with two antibiotics: Omeprazole 20 mg, amoxicillin 750 mg, and clarithromycin 7.5 mg/kg body weight together, twice daily for one week

>40 kg	In combination with two antibiotics: Omeprazole 20 mg, 1 gamoxicillin and clarithromycin 500 mg together, twice a day for one week

Special patient groups *Kidney damage*
No dose adjustment is necessary in patients with impaired renal function (see section 5.2).

Liver damage
In patients with impaired liver function, a daily -dose of 10 to 20 mg may be sufficient. (See point 5.2).

Elderly people
It is not necessary to modify the dose in the elderly (see section 5.2).

Method of application
It is recommended to take the Omeprazole capsule whole, with half a glass of water, in the morning. The capsules should not be chewed or crushed.

For patients with swallowing difficulties and children who can already consume liquid or semi-solid food
The patient can open the capsule and its contents in half a glass of water or a slightly acidic liquid, e.g. you can also take it mixed in fruit juice, applesauce or non-carbonated mineral water. The patient's attention should be drawn to the fact that the dispersion must be consumed immediately (or within 30 minutes) and that the dispersion must always be stirred immediately before ingestion and then washed down with half a glass of water.

Another way: after sucking the capsule, the pellets inside should be swallowed with half a glass of water. Enteric pellets should not be chewed.

4.3 Contraindications
- Hypersensitivity to the active ingredient of the preparation, substituted benzimidazole or any of the excipients listed in point 6.1.
- Omeprazole, -like other proton pump inhibitors (PPIs), cannot be given together with nelfinavir (see section 4.5).

4.4 Special warnings and precautions for use
Malignancy should be ruled out in the presence of any warning symptoms (e.g. significant, unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena) and in the presence or suspicion of a gastric ulcer, as treatment may mask the symptoms and thus delay the diagnosis.

Concomitant use of atazanavir with proton pump inhibitors is not recommended (see section 4.5). -If the combined use of atazanavir and a proton pump inhibitor is deemed necessary, close clinical monitoring (e.g. the level of virus in the body) is recommended - with the use of an increased dose of atazanavir to 400 mg and a combination of 100 mg ritonavir; the dose of esomeprazole 20 mg should not be exceeded.

Like any medicine that inhibits acid production, omeprazole can also reduce the absorption of vitamin B 12 (cyanocobalamin), which is caused by reduced stomach acid production or its complete absence. This should be taken into account in patients whose body stores a reduced amount of vitamin B 12, or who have risk factors that result in inadequate absorption of vitamin B 12 during long-term therapy.

Omeprazole is a CYP2C19 inhibitor. When starting and ending treatment with

omeprazole, possible interactions with drugs metabolized by the CYP2C19 enzyme should be taken into account. A drug- drug interaction has been observed between omeprazole and clopidogrel (see section 4.5). The clinical significance of this interaction is not yet clear. As a precaution, co-administration of omeprazole and clopidogrel is not recommended.

Severe hypomagnesaemia has been reported in patients treated with proton pump inhibitors such as omeprazole for at least 3 months and in most cases for a year. Hypomagnesaemia can present with severe symptoms such as exhaustion, tetany, delirium, convulsions, dizziness, ventricular arrhythmias, which symptoms often begin unnoticed and are initially ignored. Hypomagnesaemia improved in most affected patients with magnesium replacement therapy and discontinuation of proton pump inhibitors. Physicians should consider monitoring magnesium levels prior to initiation of treatment and at regular intervals during treatment in patients who are expected to receive long-term proton pump inhibitor therapy or who are concurrently taking digoxin or medications that may cause hypomagnesaemia (e.g., diuretics).

Rarely and very rarely, serious skin reactions (SCARs), including Stevens−Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with omeprazole treatment. , which can be life-threatening or fatal.

Proton pump inhibitors, especially in high doses and long-term use (more than 1 year), may moderately increase the risk of hip, wrist, and spine fractures, especially in the elderly or in patients with other known risk factors. According to observational studies, proton pump inhibitors -increase the risk of fractures by 10-40%. Other risk factors may partly contribute to the increase in risk.
Patients at risk of osteoporosis should receive care in accordance with current clinical guidelines and adequate vitamin D and calcium intake.

Sub acute cutaneous lupus erythematosus (SCLE)
Proton pump -inhibitors is very rarely associated with cases of SCLE. In case of changes, especially if this is in an area of the skin exposed to the sun, as well as if it is associated with joint pain, you should urgently consult a doctor and consider stopping the administration of Omeprazole. The occurrence of SCLE during previous treatment with a proton pump inhibitor may increase the chance of SCLE with the use of other proton pump inhibitors.

Kidney damage
Acute tubulointerstitial nephritis (TIN), which may occur at any time during omeprazole treatment, has been observed in patients taking omeprazole (Section 4.8). Acute tubulointerstitial nephritis can progress to renal failure.
If TIN is suspected, the use of omeprazole should be stopped and appropriate treatment should be started immediately.

Disturbing effect on laboratory tests
Elevated chromogranin-A (CgA) levels may interfere with neuroendocrine tumor investigations. In order to avoid this interaction, treatment with Omeprazole gastric juice-resistant hard capsules should be stopped at least 5 days before the CgA measurement (see section 5.1). If the CgA -and gastrin levels do not return to the reference range after the original measurement, -the measurement must be repeated 14 days after stopping the proton pump inhibitor treatment.
In the case of some children with chronic diseases, long-term treatment may become necessary, but this is not recommended.

Omeprazole contains lactose. The product cannot be taken in rare cases of hereditary galactose intolerance, complete lactase -deficiency or glucose- galactose malabsorption.- proton pump -inhibitors may slightly increase certain gastrointestinal infections, such as the risk of Salmonella or *Campylobacter infection, and possibly also the risk of Clostridium difficile infection* in patients receiving hospital care (see section 5.1).

In the case of any long-term treatment, especially if its duration exceeds one year, the patient must be regularly and closely monitored.

Omeprazole capsules contain less than 1 mmol sodium (23 mg) per capsule, i.e. practically 'sodium-free'.

4.5 Drug interactions and other interactions

Effect of omeprazole on the pharmacokinetics of other active substances

Active ingredients that are absorbed depending on the pH

Due to reduced intragastric acidity during omeprazole treatment, the absorption of absorbed active substances may increase or decrease depending on the pH.

Nelfinavir, atazanavir

Plasma concentrations of nelfinavir and atazanavir are reduced when co-administered with omeprazole.

Co-administration of omeprazole with nelfinavir is contraindicated (see section 4.3).
When omeprazole (40 mg daily) is co-administered, the average exposure of nelfinavir is approx. by 40% -, and the average exposure of the pharmacologically active M8 metabolite decreased by 7590%. CYP2C19 inhibition may also play a role in the interaction.

The combined use of omeprazole and atazanavir is not recommended (see section 4.4) reduced atazanavir exposure by 75% in healthy volunteers. -Increasing the atazanavir dose to 400 mg did not compensate for the effect of omeprazole on atazanavir exposure. In healthy volunteers (20 mg daily) omeprazole and 400 mg atazanavir/100 mg ritonavir combined resulted in an approximately 30% reduction in atazanavir exposure compared to exposure observed with 300 mg atazanavir/100 mg ritonavir daily.

Digoxin

When omeprazole (20 mg per day) and digoxin were used together in healthy subjects, the bioavailability of digoxin -increased by 10%. Digoxin toxicity has rarely been reported. However, caution is required when using omeprazole in high doses in elderly patients. In such cases, therapeutic drug level monitoring of digoxin should be introduced.

Clopidogrel

The results of studies in healthy subjects showed a pharmacokinetic/pharmacodynamic interaction between clopidogrel (300 mg -loading dose/75 mg daily maintenance dose) and omeprazole (80 mg orally per day *) , resulting in an average 46%* reduction in exposure to the active metabolite of clopidogrel , -and resulted in an average 16% reduction in the maximum inhibition of platelet aggregation (ADP induced).

Conflicting data have been reported from both observational and clinical studies on the clinical effect of the pharmacokinetic/pharmacodynamic interaction of omeprazole on major cardiovascular events. As a precaution, co-administration of omeprazole and clopidogrel is not recommended (see section 4.4).

Other active ingredients
Absorption of posaconazole, erlotinib, ketoconazole and itraconazole is significantly reduced and thus clinical efficacy may be reduced. Co-administration with posaconazole and erlotinib should be avoided.

Active substances metabolized by the CYP2C19 enzyme
Omeprazole moderately inhibits the activity of CYP2C19, which plays a major role in the metabolism of omeprazole. Thus, when co-administered with active substances that are also metabolized by the CYP2C19 enzyme, their metabolism may slow down and their systemic exposure may increase. Such medicinal products, e.g. R -warfarin and the other vitamin K antagonist's cilostazol, diazepam and phenytoin.

Cilostazol
max) of cilostazol increased by 18% -, the area under the curve (AUC, area under the curve) of the time- plasma concentration by 26%, and the C max value of one of its active metabolites increased as a result of 40 mg omeprazole administered to healthy subjects. 29% -, and the AUC value increased by 69%.

Phenytoin
Monitoring of phenytoin plasma concentration is recommended when introducing omeprazole therapy during the first two weeks and when modifying the phenytoin dose. When omeprazole therapy ends, it is also necessary to check and make another dose adjustment.

Unknown mechanism

Saquinavir
Co-administration of omeprazole with saquinavir/ritonavir resulted in an approximately 70% increase in saquinavir plasma concentration -, which was well tolerated by HIV-infected patients.

Tacrolimus
With the use of omeprazole, an increase in the blood level of tacrolimus has been reported. Tacrolimus plasma concentration and renal function (creatinine -clearance) should be closely monitored and the tacrolimus dose adjusted if necessary.

Methotrexate
Elevated methotrexate levels have been reported in some patients when -given concomitantly with proton pump inhibitors (PPIs). When using high-dose methotrexate, temporary suspension of omeprazole treatment may need to be considered.

Effect of other active substances on the pharmacokinetics of omeprazole

CYP2C19 and/or CYP3A4 inhibitors
Since omeprazole is metabolised by the CYP2C19 and CYP3A4 enzymes, known CYP2C19 or CYP3A4 inhibitors (such as clarithromycin or voriconazole) -may result in an increase in omeprazole serum levels due to a reduction in the rate of omeprazole metabolism. More than twice the exposure of omeprazole was observed when co-administered with voriconazole. Because high doses of omeprazole are well tolerated, no dose adjustment of omeprazole is usually necessary. However, in patients with severe liver damage, or if long-term treatment is indicated, dose modification should be considered.

CYP2C19 and/or CYP3A4 inducers

Known inducers of CYP2C19 or CYP3A4, or inducers of both enzymes (such as rifampicin and St. John's Wort), may result in decreased serum levels of omeprazole by accelerating the metabolism of omeprazole.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy
Data from three prospective epidemiological studies (more than 1,000 known outcomes) do not suggest that omeprazole has harmful effects on pregnancy or the foetus/neonate. Omeprazole can also be used during pregnancy.

Breast-feeding
Omeprazole is excreted in breast milk, but at therapeutic doses it is unlikely to affect the child.

Fertility
Animal studies with orally administered omeprazole racemic mixture do not indicate effects on fertility.

4.7 The effects of the preparation on the abilities required for driving and operating machinery

Omeprazole is unlikely to affect the ability to drive or use machines. Drug side effects, such as dizziness and visual disturbances may occur (see section 4.8). If the patient experiences this, he must not drive a car or work with machines.

4.8 Undesirable effects, side effects

Summary of the drug safety profile
The most common side effects (in 1 to 10% of patients -) are headache, abdominal pain, constipation, diarrhea, flatulence, and nausea/vomiting.
Serious skin reactions (SCAR), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP) have been reported in association with omeprazole treatment (see section 4.4). .

Tabular list of side effects
In clinical trials with omeprazole and during post-marketing use, the following adverse drug reactions have been confirmed or suspected to be related to the treatment. None were dose dependent. The side effects listed below are grouped by frequency and system organ class. Frequency categories were defined using the following conventions: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1 /10,000 - <1/1,000), very rare (<1/10,000), not known (the frequency cannot be determined from the available data).

System Organ Class/Frequency	**Side effect**
Hematopoietic and lymphatic system diseases and symptoms	
Rare:	leukopenia, thrombocytopenia
Very rare:	agranulocytosis, pancytopenia
Immune system diseases and symptoms	
Rare:	hypersensitivity reactions, e.g. fever, angioedema, anaphylactic reaction/shock
Metabolic and nutritional diseases and symptoms	
Rare:	hyponatraemia

Not known:	hypomagnesaemia; severe hypomagnesaemia may be associated with hypocalcaemia; hypomagnesaemia can also be associated with
Psychiatric symptoms	
Infrequent:	insomnia

System Organ Class/Frequency	**Side effect**
Rare:	Agitation, Confusion, Depression
Very rare:	Aggression, Hallucinations
Nervous system diseases and symptoms	
Frequent:	Headache
Infrequent:	Dizziness, Paraesthesia, Somnolence
Rare:	Taste Disturbances
Eye diseases and ophthalmic symptoms	
Rare:	Blurred Vision
Diseases and symptoms of the ear and balance sensor	
Infrequent:	Vertigo
Respiratory, thoracic and mediastinal diseases and symptoms	
Rare:	Bronchospasm
Digestive system diseases and symptoms	
Frequent:	Abdominal Pain, Constipation, Diarrhoea, Flatulence, Nausea/Vomiting, Fundic Gland Polyps (Benign)
Rare:	Dry Mouth, Stomatitis, Gastrointestinal Candidiasis
Not known:	Microscopic Colitis
Liver and biliary diseases and symptoms	
Infrequent:	Elevated Liver Enzymes
Rare:	Hepatitis With Or Without Jaundice
Very rare:	Liver Failure, Encephalopathy In Patients With Pre-Existing Liver Disease
Diseases and symptoms of the skin and subcutaneous tissue	
Infrequent:	Dermatitis, Pruritus, Rash, Urticaria
Rare:	Alopecia, Photosensitivity, Acute Generalized Exanthematous Pustulosis (AGEP), Drug Reaction With Eosinophilia And Systemic Complaints (DRESS)
Very rare:	Erythema Multiforme, Stevens–Johnson Syndrome, Toxic Epidermal Necrolysis (TEN)
Not known	Sub acute Cutaneous Lupus Erythematosus (See
Diseases and symptoms of the musculoskeletal system and connective tissue	
Infrequent:	Hip, Wrist Or Spine Fractures
Rare:	Arthralgia, Myalgia
Very rare:	Muscle Weakness
Kidney and urinary tract diseases and symptoms	
Rare:	Tubulointerstitial nephritis (can progress to kidney
Diseases and symptoms related to the genital organs and breasts	
Very rare:	Gynecomastia
General symptoms, application site reactions	
Infrequent:	General Malaise, Peripheral Oedema
Rare:	Increased Sweating

Children and adolescents

The safety of omeprazole -was studied in a total of 310 children between 0 and 16 years of age with diseases related to gastric acid production. There are limited data on the safety of

long-term use from a clinical trial in which 46 children with severe erosive esophagitis received omeprazole maintenance therapy for 749 days. The profile of adverse events was generally similar to that seen in short- and long-term treatment in adults. There are no long-term data on the effects of omeprazole on puberty and growth.

Reporting suspected side effects
After the authorization of the drug, it is important to report suspected side effects, because means of continuously monitoring the benefit/risk profile of the drug. Healthcare professionals are requested to report suspected side effects to the authority via

4.9 Overdose

Limited data are available on the effects of omeprazole overdose in humans. Doses up to 560 mg have been described in the literature -, and single oral doses of omeprazole have been reported *to* reach 2400 mg (120 times the usual recommended clinical dose). Nausea, vomiting, dizziness, abdominal pain, diarrhea and headache have been reported as a consequence of omeprazole overdose. Apathy, depression and confusion also occurred in some cases.

The described symptoms were transient and no case with a serious outcome was reported. The rate of elimination remained unchanged at increased doses (first-order kinetics). Treatment, if necessary, is symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: drugs for diseases associated with acid production disorders, proton pump -inhibitors,
ATC code: A02BC01

Mechanism of action
Omeprazole, which is a racemic mixture of two enantiomeric molecules, -reduces gastric acid secretion through a targeted action mechanism. It is a special inhibitor of the proton pump in the parietal cell. It acts quickly and ensures acid control by reversibly inhibiting gastric acid secretion with a once-daily dose.

Omeprazole is a weak base that is concentrated and activated in the acidic environment of the intracellular canaliculus of the parietal cell, where it inhibits the H^+, K^+ -ATPase enzyme, i.e. the function of the proton pump. Its effect on the last phase of gastric acid formation is dose-dependent and very effectively inhibits both basal and stimulated acid production, regardless of stimulation.

Pharmacodynamic effects
All observed pharmacodynamic effects can be explained by the effect of omeprazole on acid secretion.

Effect on gastric acid secretion-
Once -daily oral dose of omeprazole quickly and effectively inhibits both daytime and nighttime gastric acid secretion; it reaches its maximum effect within 4 days after the start of therapy. With 20 mg of omeprazole, an average reduction of at least 80% of the intragastric acidity of duodenal ulcer patients can be maintained for 24 hours -. 24 hours after the administration of the dose, the average decrease in the peak of acid production following pentagastrin stimulation is at least 70%.

In patients with duodenal ulcer, a 20 mg dose of omeprazole -maintains intragastric pH ≥ 3 for an average of 17 hours out of a 24-hour period.

Due to reduced acid secretion and intragastric acidity, omeprazole -dose-dependently reduces/normalizes the acid exposure of the esophagus in patients with gastro-oesophageal reflux. The inhibition of acid secretion is not proportional to the instantaneous value of the plasma concentration, but to the area under the curve (AUC) of the omeprazole time-plasma concentration function.

Tachyphylaxis was not experienced during omeprazole treatment.

Effect on H. pylori-
H. *pylori* infection is associated with peptic ulcer disease in both the duodenum and the stomach. H. *pylori* is a significant factor in the development of gastritis. Together, H. *pylori* and stomach acid play an important role in the development of peptic ulcer disease. H. *pylori* is the main cause of the development of atrophic gastritis, which carries an increased risk of gastric cancer.

H. pylori eradication with omeprazole and an antimicrobial agent, there is a good cure rate and long- term remission of peptic ulcer.

When dual therapies were examined, they were found to be less effective than triple combinations. At the same time, their use should be considered in cases where known hypersensitivity precludes the use of any triple combination.

Other -effects related to inhibition of acid secretion
Glandular cysts in the stomach occurred slightly more often during long-term treatment. These are -benign physiological changes that appear to be reversible as a result of strong inhibition of acid secretion.

A decrease in stomach acid for any reason, including the use of proton pump inhibitors, results in an increase in the number of bacteria in the stomach that are normally present in the gastrointestinal tract. Acid-reducing therapy may slightly increase certain gastrointestinal infections, such as the risk of developing Salmonella or *Campylobacter infection, and possibly also the risk of Clostridium difficile infection* in patients receiving hospital care.

During treatment with antisecretory drugs, serum gastrin levels rise in response to decreased acid secretion. Due to the reduced acidity of the stomach, CgA also rises. Elevated CgA -levels may interfere with neuroendocrine tumor investigations.
Available published evidence suggests that proton pump inhibitors -should be discontinued for 5 days and 2 weeks before CgA measurements. -This allows the -possibly falsely elevated CgA -level to return to the reference range after PPI treatment.

Long-term omeprazole -treatment, an increase in the number of ECL (*enterochromaffin -like)* cells, probably associated with elevated serum gastrin levels, was observed in some patients (both children and adults). The results are considered to have no clinical significance.

Children and adolescents
In an uncontrolled study in children (1 -to 16 years) with severe reflux esophagitis, omeprazole administered at a dose of 0.71.4 mg/kg resulted in improvement of esophagitis in 90% of cases and significantly reduced reflux symptoms. In a simple study,

024-month-old children with clinically diagnosed gastroesophageal reflux disease were treated with 0.5 mg/kg, 1.0 mg/kg, or 1.5 mg/kg of omeprazole. Regardless of the size of the applied dose, the frequency of vomiting/regurgitation -decreased by 50% after the 8th week of treatment.

Eradication of H. pylori in children
A randomized double- -blind clinical trial (Héliot trial) established the efficacy and safety of omeprazole used in combination with two antibiotics (amoxicillin and clarithromycin) in the treatment of *H. pylori* infection in children aged 4 years and older with gastritis: the *H. pylori* eradication rate is omeprazole + in the amoxicillin + clarithromycin group it was 74.2% (23/31 patients), while in the amoxicillin + clarithromycin group it was 9.4% (3/32 patients). However, no clinical benefit has been demonstrated with regard to dyspepsia symptoms. The results of this study cannot be applied to children under the age of four.

5.2 Pharmacokinetic properties

Absorption
Omeprazole and omeprazole -magnesium break down under the action of acid, so they are used in the form of capsules or tablets consisting of enteric-coated granules. Omeprazole is rapidly absorbed, with peak plasma concentrations occurring approximately 12 hours after dosing. Omeprazole is absorbed from the small intestine, usually within 36 hours. Simultaneous food intake does not affect bioavailability. After a *single oral dose*, the systemic utilization (bioavailability) of omeprazole is approx. 40%. After repeated, once-daily dosing, the bioavailability is approx. rises to 60%.-

Distribution
In healthy individuals, the apparent volume of distribution is approx. 0.3 l/kg. The plasma protein binding of omeprazole is approx. 97 -%

Biotransformation
Omeprazole is completely metabolized by the cytochrome P450 enzyme system (CYP). The main part of its metabolism depends on the polymorphically defined CYP2C19 enzyme responsible for the formation of the main plasma metabolite, hydroxy omeprazole. -The remainder, another specific isoform, is a function of CYP3A4 responsible for the formation of omeprazole sulfone. Due to the strong affinity of omeprazole to the CYP2C19 enzyme, there is a possibility of competitive inhibition with other substrates of the CYP2C19 enzyme and metabolic drug-drug interaction. However, due to its weak binding to the CYP3A4 enzyme, omeprazole does not inhibit the metabolism of other CYP3A4 substrates. In addition, omeprazole does not inhibit the most important CYP enzymes.

About 3% of the Caucasian population -and approximately 1520% of the Asian population lack the functioning CYP2C19 enzyme, they are called slow metabolizers. In these individuals, the metabolism of omeprazole is likely to be primarily catalyzed by CYP3A4. After repeated administration of omeprazole 20 mg once daily, the mean AUC was approximately 510-fold higher in poor metabolisers than in subjects with a functional CYP2C19 enzyme (extensive metabolisers). The average peak plasma concentrations also increased by about 35 times. These results have no relevance to the dosing of omeprazole.

Elimination
The plasma elimination half-life of omeprazole -is usually less than one hour after both single and repeated *oral doses once daily.* Omeprazole is completely eliminated from the plasma between consecutive doses, and does not show a tendency to accumulate with once-daily administration.
Almost 80% of an oral dose of omeprazole -is excreted in the urine in the form of

metabolites, and the remainder is eliminated primarily through bile secretion, with feces.

Linearity/non-linearity
The AUC value of omeprazole increases with repeated administration. This increase is dose-dependent and -results in a non-linear dose AUC increase after repeated dosing. This time and dose dependence can be attributed to a decrease in first pass metabolism and systemic clearance, which is probably caused by omeprazole and/or its metabolites (e.g. sulfone) by inhibiting the CYP2C19 enzyme.
Metabolites have no effect on gastric acid -secretion.

Special patient groups

Liver damage
Metabolism of omeprazole is reduced in impaired liver function, resulting in an increase in AUC. Omeprazole does not show a tendency to accumulate when administered once a day.

Kidney damage
The pharmacokinetics of omeprazole, such as systemic bioavailability and rate of elimination, are not altered in patients with impaired renal function.

Elderly people
The metabolism of omeprazole is somewhat reduced in elderly individuals (75 -to 79 years).

Children and adolescents
In children older than 1 year, plasma concentrations similar to those of adults developed during therapy with the dosage recommended for children. Omeprazole clearance is low in infants younger than 6 months due to immature omeprazole metabolism.

5.3 Results of preclinical safety studies
In lifelong studies, gastric ECL -cell hyperplasia and the appearance of carcinoids were observed in rats treated with omeprazole. These changes develop as a result of persistent hypergastrinemia due to inhibition of acid secretion. Similar changes were experienced after treatment with H_2 receptor antagonists, proton pump inhibitors and partial fundectomy. -Thus, these changes are not the result of a direct effect of a certain drug.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients

Mannitol
Sucrose
Disodium Hydrogen Phosphate
Calcium Carbonate
Sodium Lauryl Sulphate
Hypromellose
Methacrylic Acid and ethyl Acrylate copolymer dispersion
Diethyl Phthalate
Titanium Dioxide
Purified Talc
N.P. Seeds

6.2 Incompatibilities
Not applicable.

6.3 Shelf Life

3 years.

6.4 Special storage requirements

Store at a temperature not exceeding 30 °C, protect from moisture.
Keep out of reach of children

6.5 Type of packaging and packaging

1x10 Capsules in Alu-Alu blister pack. Such 10 blisters are packed in carton along with insert.

6.6 Special precautions for disposal and other information related to the handling of the preparation

There are no special requirements.
Any unused medicine or waste material must be disposed of in accordance with the regulations for medicines.

Note: Classification: **II. Group**
Medicine subject to medical prescription only (V).

7. MARKETING AUTHORIZATION HOLDER

Zim Laboratories Limited.
Sadoday Gyan (Ground Floor),
Opp. NADT, Nelson Square,
Nagpur – 440013
India.

8. MARKETING AUTHORIZATION NUMBER(S)

05108/07294/NMR/2019

9. DATE OF FIRST ISSUANCE/RENEWAL OF THE MARKETING AUTHORIZATION

13/04/2020

10. DATE OF CHECK OF THE TEXT

02/07/2023