1.1 Name of the medicinal product:
FAMA OMEPRAZOLE
(Gastro-resistant Omeprazole Capsules BP 20 mg)

1.2 Qualitative and quantitative composition:
Each Capsule Contains:
Omeprazole (as enteric coated pellets) 20 mg
Approved Colour Used in pellets and Empty Capsule Shell.

Sr. No.	Ingredients	Specifi-cation	Label Claim / Capsule (In mg)	Over-ages added (In %)	Qty. / Capsule (In mg)	Reason for Function
1.	Omeprazole (As enteric coated pellets)	In-House	20.00	NA	Omeprazole enteric coated pellets 267.00 mg equivalent to Omeprazole 20.00mg	Medicament
2.	EHG Capsule Size`2` Cap-Pink Body-Clear Transparent	In-House	NA	NA	1 Capsule = 63.00 mg	Capsule Shell
	Net Content/Capsule (In mg)				**267.00**	
	Weight of empty capsule shell (In mg)				**63.00**	
	Average weight of filled capsule (In mg)				**330.00**	

1.3 Pharmaceutical form: Capsules
Description: Pink coloured cap & Clear transparent body of capsule size 2, containing white pellets.

4 Clinical particulars
4.1 Therapeutic indications
FAMA OMEPRAZOLE is indicated in-
1. Treatment of reflux oesophagitis disease. In reflux oesophagitis the majority of patients are healed after 4 weeks. Symptom relief is rapid.
2. Treatment of duodenal and benign gastric ulcers including complicating NSAID therapy.
3. Relief of reflux-like symptoms (e.g. heartburn) and/or ulcer-like symptoms (e.g. epigastric pain) associated with acid-related dyspepsia.
4. Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and gastro duodenal erosions in patients with a previous history of gastro duodenal lesions that require continued NSAID treatment.
5. Relief of associated dyspeptic symptoms.
6. Helicobacter pylori eradication: When used with in combination with antibiotics, Omeprazole proves effective in the eradication of *Helicobacter pylori* (*Hp*) in peptic ulcer disease.
7. Prophylaxis of acid aspiration.
8. Zollinger-Ellison syndrome.

4.2 Posology and method of administration

Route: oral

Oesophageal reflux disease including reflux oesophagitis:

The usual starting dose is 20 mg Omeprazole taken once a day for 4 weeks. For those patients not fully healed after the initial 4 week course, healing usually occurs during a further 4-8 weeks treatment.

Omeprazole has also been used in a dose of 40mg once a day in patients with reflux oesophagitis refractory to other therapy. Healing usually occurred within 8 weeks. Continuation of therapy can be considered at a dosage of 20 mg once daily.

Acid reflux disease:

For long-term management, a dose of 10 mg once daily is recommended, increasing to 20 mg if symptoms return.

Duodenal and benign gastric ulcers:

The usual dose is 20 mg Omeprazole once daily. With duodenal ulcers, the majority of patients usually are healed after 4 weeks of treatment. The majority of patients with benign gastric ulcer are healed after 8 weeks. In severe or recurrent cases the dose may be increased to 40 mg Omeprazole daily. For patients with a history of recurrent duodenal ulcer, long term therapy is recommended at a dosage of 20 mg omeprazole once daily.

To prevent recurrence, in patients with duodenal ulcer, the recommended dose is omeprazole 10 mg, once daily, increasing to 20 mg, once daily if symptoms return.

The following groups of patients are at risk from recurrent ulcer relapse: those with *Helicobacter pylori* infection, younger patients (<60 years), those symptoms persist for more than one year and smokers. These patients will require initial long-term therapy with omeprazole 20 mg once daily, reducing to 10 mg once daily, if necessary.

Acid-related dyspepsia:

Usual dosage is 10 mg or 20 mg Omeprazole once daily for 2 - 4 weeks depending on the severity and persistence of symptoms.

If the patient does not respond to treatment after 4 weeks or who relapse shortly after treatment, then the patient should be investigated.

For the treatment of NSAID-associated gastric ulcers, duodenal ulcers or gastroduodenal erosions:

The recommended dosage of Omeprazole is 20 mg once daily. Symptom resolution is rapid and in most patients healing occurs within 4 weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further 4 weeks treatment.

For the prophylaxis of NSAID-associated gastric ulcers, duodenal ulcers, gastroduodenal erosions and dyspeptic symptoms in patients with a previous history of gastroduodenal lesions who require continued NSAID treatment:

The recommended dosage is 20 mg Omeprazole taken once a day.

***Helicobacter pylori (Hp)* eradication regimens in peptic ulcer disease:**

Omeprazole is recommended at a dose of 40 mg once daily or 20 mg twice daily concomitant with antimicrobial agents as detailed below:

Triple therapy regimens in duodenal ulcer disease:

Omeprazole and the following antimicrobial combinations; Amoxicillin 500 mg and Metronidazole 400 mg both three times a day for one week. Or Clarithromycin 250 mg and Metronidazole 400 mg (or Tinidazole 500 mg) both twice a day for one week. Or Amoxicillin 1 g and Clarithromycin 500 mg both twice a day for one week.

Dual therapy regimens in duodenal ulcer disease

Omeprazole and Amoxicillin 750 mg to 1 g twice daily for two weeks. Alternatively, Omeprazole and Clarithromycin 500 mg three times a day for two weeks.

Dual therapy regimens in gastric ulcer disease:
Omeprazole and Amoxicillin 750 mg to 1 g twice daily for two weeks. In each regimen if symptoms return and the patient tests positive for *Hp*, therapy may be repeated or one of the alternative regimens can be used; if the patient is *Hp* negative then see dosage instructions for acid reflux disease.
To ensure healing in patients with active peptic ulcer disease, see further dosage recommendations for duodenal and benign gastric ulcer.
Prophylaxis of acid aspiration:
For patients considered to be at risk of aspiration of the gastric contents during general anaesthesia, the recommended dosage is Omeprazole 40 mg on the evening before surgery followed by a further 40 mg 2 - 6 hours prior to surgery.
Zollinger-Ellison syndrome:
The initial starting dose is Omeprazole 60 mg once a day. The dosage should be adjusted individually and treatment continued as long as clinically indicated. More than 90% of patients with severe disease and inadequate response to other therapies have been effectively controlled on doses of 20-120 mg daily. With doses above 80 mg daily, the dose should be divided and given twice daily.
Elderly:
Dose adjustment is not required in the elderly.
Children
Reflux oesophagitis
The treatment time is 4-8 weeks.
Symptomatic treatment of heartburn and acid regurgitation in gastroesophageal reflux Disease.
The treatment time is 2-4 weeks. If symptom control has not been achieved after 2-4 weeks the patient should be investigated further.
The dosage recommendations are as follows:

Age	Weight	Dosage
1 year of age	10-20 kg	10 mg once daily. The dosage can be increased to 20 mg once daily if needed.
2 years of age	> 20 kg	20 mg once daily. The dosage can be increased to 40 mg once daily if needed.

Children over 4 years of age
In combination with antibiotics in treatment of duodenal ulcer caused by Helicobacter pylori. When selecting appropriate combination therapy consideration should be given to official local guidance regarding bacterial resistance, duration of treatment (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents. The treatment should be supervised by a specialist.
Weight Dosage

15- 30kg	Combination with two antibiotics: Omeprazole 10 mg, amoxicillin
25mg/kg	body weight and Clarithromycin 7.5 mg/kg body weight are all administered together 2 times daily for 1 week
30- 40kg	Combination with two antibiotics: Omeprazole 20 mg, amoxicillin750 mg and clarithromycin 7.5 mg/kg body weight are all administered 2 times daily for 1 week.
>40 kg	Combination with two antibiotics: Omeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg are all administered 2 times daily for 1 week.

Impaired renal function:
Dose adjustment is not required in patients with impaired renal function.
Impaired hepatic function:
As bioavailability and half-life can increase in patients with impaired hepatic function, the dose requires adjustment with a maximum daily dose of 20 mg.
For patients (including children aged 1 year and above who can drink or swallow semi-solid food) who are unable to swallow omeprazole Capsules:
The capsules may be opened and the contents swallowed directly with half a glass of water or suspended in 10 ml of non-carbonated water, any fruit juice with a pH less than 5 e.g. apple, orange, pineapple, or in applesauce or yoghurt and swallowed after gentle mixing. The dispersion should be taken immediately or within 30 minutes. Stir just before drinking and rinse it down with half a glass of water. Alternatively the actual capsules may be sucked and then swallowed with half a glass of water. There is no evidence to support the use of sodium bicarbonate buffer as a delivery form. It is important that the contents of the capsules should not be crushed or chewed.

4.3 Contraindications
FAMA OMEPRAZOLE is contraindicated in patients with known hypersensitivity to substituted benzimidazoles or to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, interstitial nephritis, and urticaria.

4.4 Special warnings and precautions for use
Clostridium difficile associated diarrhea
Published observational studies suggest that PPI therapy like Omeprazole may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents. For more information specific to antibacterial agents indicated for use in combination with Omeprazole.
Interaction with clopidogrel
Avoid concomitant use of Omeprazole with clopidogrel. Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as omeprazole, that inhibit CYP2C19 activity. Concomitant use of clopidogrel with 80 mg omeprazole reduces the pharmacological activity of clopidogrel, even when administered 12 hours apart. When using Omeprazole, consider alternative anti-platelet therapy.
Bone fracture
Several published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.
Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically

Concomitant use of Omeprazole With St. John's Wort or rifampin

Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease omeprazole concentrations. Avoid concomitant use of Omeprazole with St. John's Wort or rifampin.

Interactions with diagnostic investigations for neuroendocrine tumors

Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Healthcare providers should temporarily stop omeprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g. for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Concomitant Use Of Omeprazole with methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may be considered in some patients.

Concomitant gastric malignancy

Symptomatic response to therapy with Omeprazole does not preclude the presence of gastric malignancy.

Atrophic gastritis

Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole.

Acute interstitial nephritis

Acute interstitial nephritis has been observed in patients taking PPIs including Omeprazole Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue Omeprazole if acute interstitial nephritis develops

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. Rare reports of cyanocobalamin deficiency occurring with acidsuppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

4.5 Interaction with other medicinal products and other forms of interaction

Interference with antiretroviral therapy

Concomitant use of atazanavir and nelfinavir with proton pump inhibitors is not recommended. Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance. Coadministration of saquinavir with proton pump inhibitors is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction.

Omeprazole has been reported to interact with some antiretroviral drugs. The clinical importance and the mechanisms behind these interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral drug. Other possible interaction mechanisms are via CYP 2C19.

Reduced concentrations of atazanavir and nelfinavir
For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. Following multiple doses of nelfinavir (1250 mg, twice daily) and omeprazole (40 mg daily), AUC was decreased by 36% and 92%, Cmax by 37% and 89% and Cmin by 39% and 75% respectively for nelfinavir and M8. Following multiple doses of atazanavir (400 mg, daily) and omeprazole (40 mg, daily, 2 hr before atazanavir), AUC was decreased by 94%, Cmax by 96%, and Cmin by 95%. Concomitant administration with omeprazole and drugs such as atazanavir and nelfinavir is therefore not recommended.
Increased concentrations of saquinavir
For other antiretroviral drugs, such as saquinavir, elevated serum levels have been reported, with an increase in AUC by 82%, in Cmax by 75%, and in Cmin by 106%, following multiple dosing of saquinavir/ritonavir (1000/100 mg) twice daily for 15 days with omeprazole 40 mg daily co-administered days 11 to 15. Therefore, clinical and laboratory monitoring for saquinavir toxicity is recommended during concurrent use with Omeprazole. Dose reduction of saquinavir should be considered from the safety perspective for individual patients. There are also some antiretroviral drugs of which unchanged serum levels have been reported when given with omeprazole.

4.6 Pregnancy and Lactation:
Pregnancy: There have been no human studies completed on the effect of Omeprazole on pregnancy or fetal health. Animal studies have shown evidence of lethality to embryos and fetal toxicity. Animal studies are not necessarily reflective of effect in humans, but due to the potential for side effects Omeprazole should only be used during pregnancy when benefits outweigh risks. Omeprazole has been successfully given to women hours before birth for the prevention of Mendelson's syndrome. Mendelson's syndrome occurs when pregnant patients aspirate blood, gastric juice, water or bile after having anesthesia.

Lactation: Omeprazole has been given to infants at doses of 1 mg/kg daily. While the drug does pass to the infant via breast milk, the amount ingested by infants is estimated at about 3 mcg/kg daily– a fraction of the prescribed amount. There have been no reported side effects in infants breastfeeding to mothers using Omeprazole.

4.7 Effects on ability to drive and use machines
FAMA OMEPRAZOLE Capsules are not likely to affect ability to drive or use any tools or machines. Side effects such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects
Common side effects
- Headache.
- Effects on your stomach or gut: diarrhoea, stomach pain, constipation, wind (flatulence).
- Feeling sick (nausea) or being sick (vomiting).

Uncommon side effects
- Swelling of the feet and ankles.
- Disturbed sleep (insomnia).
- Dizziness, tingling feelings such as "pins and needles", feeling sleepy.
- Spinning feeling (vertigo).
- Changes in blood tests that check how the liver is working.
- Skin rash, lumpy rash (hives) and itchy skin.
- Generally feeling unwell and lacking energy.

Rare side effects

- Blood problems such as a reduced number of white cells or platelets. This can cause weakness, bruising or make infections more likely.
- Allergic reactions, sometimes very severe, including swelling of the lips, tongue and throat, fever, wheezing.
- Low levels of sodium in the blood. This may cause weakness, being sick (vomiting) and cramps.
- Feeling agitated, confused or depressed.
- Taste changes.
- Eyesight problems such as blurred vision.
- Suddenly feeling wheezy or short of breath (bronchospasm).
- Dry mouth
- An inflammation of the inside of the mouth.
- An infection called "thrush" which can affect the gut and is caused by a fungus.
- Liver problems, including jaundice which can cause yellow skin, dark urine, and tiredness.
- Hair loss (alopecia).
- Skin rash on exposure to sunshine.
- Joint pains (arthralgia) or muscle pains (myalgia).
- Severe kidney problems (interstitial nephritis).
- Increased sweating.

Very rare side effects

- Changes in blood count including agranulocytosis (lack of white blood cells).
- Aggression.
- Seeing, feeling or hearing things that are not there (hallucinations).
- Severe liver problems leading to liver failure and inflammation of the brain.
- Sudden onset of a severe rash or blistering or peeling skin. This may be associated with a high fever and joint pains (Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis).
- Muscle weakness.
- Enlarged breasts in men.
- Hypomagnesaemia

4.9 Overdose

Symptoms- Reports have been received of overdosage with Omeprazole in humans. 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 normal clinical experience. Symptoms were transient, and no serious clinical outcome has been reported when Omeprazole was taken alone.

Treatment- 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.

As with the management of any overdose, the possibility of multiple drug ingestion should be considered. Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

5 Pharmacological properties

5.1 Pharmacodynamic properties

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

Effect on gastric acid secretion

Oral dosing with Omeprazole once daily provides for rapid and effective inhibition of daytime and night time gastric acid secretion with maximum effect being achieved within 4 days of treatment. With Omeprazole 20 mg, a mean decrease of at least 80% in 24-hour intragastric acidity is then maintained in duodenal ulcer patients, with the mean decrease in peak acid output after pentagastrin stimulation being about 70% 24 hours after dosing.

Oral dosing with Omeprazole 20 mg maintains an intragastric pH of ≥ 3 for a mean time of 17 hours of the 24-hour period in duodenal ulcer patients.

As a consequence of reduced acid secretion and intragastric acidity, Omeprazole dose-dependently reduces/normalizes acid exposure of the esophagus in patients with gastro-esophageal reflux disease. The inhibition of acid secretion is related to the area under the plasma concentration-time curve (AUC) of Omeprazole and not to the actual plasma concentration at a given time.

No tachyphylaxis has been observed during treatment with Omeprazole.

Effect on H. pylori

H. pylori is associated with peptic ulcer disease, including duodenal and gastric ulcer disease. H. pylori is a major factor in the development of gastritis. H. pylori together with gastric acid are major factors in the development of peptic ulcer disease. H. pylori is a major factor in the development of atrophic gastritis which is associated with an increased risk of developing gastric cancer.

Dual therapies have been tested and found to be less effective than triple therapies. They could, however, be considered in cases where known hypersensitivity precludes use of any triple combination.

Other effects related to acid inhibition

During long-term treatment gastric glandular cysts have been reported in a somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

Chromogranin A (CgA) also increases due to decreased gastric acidity. This CgA modifying effect cannot be demonstrated five days after stopping treatment with PPIs.

Omeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.

Paediatric use

In a non-controlled study in children (1 to 16 years of age) with severe reflux esophagitis, Omeprazole at doses of 0.7 to 1.4 mg/kg improved esophagitis level in 90% of the cases and significantly reduced reflux symptoms. In a single-blind study, children aged 0–24 months with clinically diagnosed gastroesophageal reflux disease were treated with 0.5, 1.0 or 1.5 mg Omeprazole/kg. The frequency of vomiting/regurgitation episodes decreased by 50% after 8 weeks of treatment irrespective of the dose.

Eradication of H. pylori in children

A randomised, double blind clinical study (Heliot study) concluded that Omeprazole in combination with two antibiotics (amoxicillin and clarithromycin), was safe and effective in the treatment of H. pylori infection in children age 4 years old and above with gastritis: H. pylori eradication rate: 74.2% (23/31 patients) with Omeprazole + amoxicillin + clarithromycin versus 9.4% (3/32 patients) with amoxicillin + clarithromycin. However, there was no evidence of

any clinical benefit with respect to dyspeptic symptoms. This study does not support any information for children aged less than 4 years.

5.2 Pharmacokinetic properties

Absorption

Omeprazole and Omeprazole magnesium are acid labile and are therefore administered orally as enteric-coated granules in capsules or tablets. Absorption of Omeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. Absorption of Omeprazole takes place in the small intestine and is usually completed within 3-6 hours. Concomitant intake of food has no influence on the bioavailability. The systemic availability (bioavailability) from a single oral dose of Omeprazole is approximately 40%. After repeated once-daily administration, the bioavailability increases to about 60%.

Distribution

The apparent volume of distribution in healthy subjects is approximately 0.3 l/kg body weight. Omeprazole is 97% plasma protein bound.

Metabolism

Omeprazole is completely metabolised by the cytochrome P450 system (CYP). The major part of its metabolism is dependent on the polymorphically expressed CYP2C19, responsible for the formation of hydroxyomeprazole, the major metabolite in plasma. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of Omeprazole sulphone. As a consequence of high affinity of Omeprazole to CYP2C19, there is a potential for competitive inhibition and metabolic drug-drug interactions with other substrates for CYP2C19. However, due to low affinity to CYP3A4, Omeprazole has no potential to inhibit the metabolism of other CYP3A4 substrates. In addition, Omeprazole lacks an inhibitory effect on the main CYP enzymes.

Approximately 3% of the Caucasian population and 15-20% of Asian populations lack a functional CYP2C19 enzyme and are called poor metabolisers. In such individuals the metabolism of Omeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 20 mg Omeprazole, the mean AUC was 5 to 10 times higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were also higher, by 3 to 5 times. These findings have no implications for the posology of Omeprazole.

Excretion

The plasma elimination half-life of Omeprazole is usually shorter than one hour both after single and repeated oral once-daily dosing. Omeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration. Almost 80% of an oral dose of Omeprazole is excreted as metabolites in the urine, the remainder in the faeces, primarily originating from bile secretion.

The AUC of Omeprazole increases with repeated administration. This increase is dose-dependent and results in a non-linear dose-AUC relationship after repeated administration. This time- and dose dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by Omeprazole and/or its metabolites (e.g. the sulphone). No metabolite has been found to have any effect on gastric acid secretion.

5.3 Preclinical safety data

Gastric ECL-cell hyperplasia and carcinoids, have been observed in life-long studies in rats treated with omeprazole. These changes are the result of sustained hypergastrinaemia secondary to acid inhibition. Similar findings have been made after treatment with H_2-receptor antagonists, proton pump inhibitors and after partial fundectomy. Thus, these changes are not from a direct effect of any individual active substance.

6 Pharmaceutical particulars

6.1 List of excipients

There are no excipients used in the formulation. Ready omeprazole pellets are directly used for encapsulation in the formulation of **FAMA OMEPRAZOLE** (Gastro-resistant Omeprazole Capsules BP 20 mg).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store below 30˚C in dry and dark place.
Keep all medicines out of reach of children.

6.5 Nature and contents of container

Packing:
Primary Packing: 1 x 14 Capsules in a strip.
Secondary Packing: 1 Strip is packed in an Inner carton along with leaflet.
Tertiary packing: Such 10 Inner cartons are packed in a outer carton. Shrink individual outer carton. Such 50 Shrinks are packed in a 5 Ply corrugated box sealed with BOPP tape & strap with strapping roll.

6.6 Special precautions for disposal and other handling

None.

7 Applicant / Manufacturer

Applicant

Applicant name and address	**M/s. BRANDS PHARMA & GENERAL ENTERPRISES,** A1 Umma Dantata Complex, Murtala Muhammad Way, Kano, Nigeria
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 , MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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