National Agency for Food & Drug Administration &Control (NAFDAC)

Registration & Regulatory Affairs (R & R)Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1 NAME OF THE MEDICINAL PRODUCT

EGMP OMEPRAZOLE CAPSULE 20mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Capsule contains:

Omeprazole	20 mg
Excipients	q.s.

3 PHARMACEUTICAL FORMS

Oral capsules

4 CLINICAL PARTICULARS

Omeprazole is indicated in:
Adults
• Treatment of duodenal ulcers
• Prevention of relapse of duodenal ulcers
• Treatment of gastric ulcers
• Prevention of relapse of gastric ulcers
• In combination with appropriate antibiotics, *Helicobacter pylori (H. pylori)* eradication in peptic ulcer disease
• Treatment of NSAID-associated gastric and duodenal ulcers
• Prevention of NSAID-associated gastric and duodenal ulcers in patients at risk
• Treatment of reflux esophagitis
• Long-term management of patients with healed reflux esophagitis
• Treatment of symptomatic gastro-oesophageal reflux disease
• Treatment of Zollinger-Ellison syndrome
Paediatric population
Children over 1 year of age and ≥ 10 kg
• Treatment of reflux esophagitis
• Symptomatic treatment of heartburn and acid regurgitation in gastro-oesophageal reflux disease
Children and adolescents over 4 years of age
• In combination with antibiotics in treatment of duodenal ulcer caused by *H. pylori*

4.2 Posology and method of administration

4.3 Posology
Adults
Treatment of duodenal ulcers
The recommended dose in patients with an active duodenal ulcer is Omeprazole 20 mg once daily. In most patients healing occurs within two weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further two weeks treatment period. In patients with poorly responsive duodenal ulcer Omeprazole 40 mg once daily is recommended and healing is usually achieved within four weeks.
Prevention of relapse of duodenal ulcers
For the prevention of relapse of duodenal ulcer in *H. pylori* negative patients or when *H. pylori* eradication is not possible the recommended dose is Omeprazole 20 mg once daily. In some patients a daily dose of 10 mg may be sufficient. In case of therapy failure, the dose can be increased to 40 mg.
Treatment of gastric ulcers
The recommended dose is Omeprazole 20 mg once daily. In most patients healing occurs within four weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further four weeks treatment period. In patients with poorly responsive gastric ulcer Omeprazole 40 mg once daily is recommended and healing is usually achieved within eight weeks.
Prevention of relapse of gastric ulcers
For the prevention of relapse in patients with poorly responsive gastric ulcer the recommended dose is Omeprazole 20 mg once daily. If needed the dose can be increased to Omeprazole 40 mg once daily.
H. pylori eradication in peptic ulcer disease

For the eradication of *H. pylori* the selection of antibiotics should consider the individual patient's drug tolerance, and should be undertaken in accordance with national, regional and local resistance patterns and treatment guidelines.
• Omeprazole 20 mg + clarithromycin 500 mg + amoxicillin 1,000 mg, each twice daily for one week, or
• Omeprazole 20 mg + clarithromycin 250 mg (alternatively 500 mg) + metronidazole 400 mg (or 500 mg or tinidazole 500 mg), each twice daily for one week or
• Omeprazole 40 mg (corresponding to 2 capsules of Omeprazole 20 mg) once daily with amoxicillin 500 mg and metronidazole 400 mg (or 500 mg or tinidazole 500 mg), both three times a day for one week.
In each regimen, if the patient is still *H. pylori* positive, therapy may be repeated.
Treatment of NSAID-associated gastric and duodenal ulcers
For the treatment of NSAID-associated gastric and duodenal ulcers, the recommended dose is Omeprazole 20 mg once daily. In most patients healing occurs within four weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further four weeks treatment period.
Prevention of NSAID-associated gastric and duodenal ulcers in patients at risk
For the prevention of NSAID-associated gastric ulcers or duodenal ulcers in patients at risk (age> 60, previous history of gastric and duodenal ulcers, previous history of upper GI bleeding) the recommended dose is Omeprazole 20 mg once daily.
Treatment of reflux esophagitis
The recommended dose is Omeprazole 20 mg once daily. In most patients healing occurs within four weeks. For those patients who may not be fully healed after the initial course, healing usually occurs during a further four weeks treatment period.
In patients with severe esophagitis Omeprazole 40 mg once daily is recommended and healing is usually achieved within eight weeks.
Long-term management of patients with healed reflux esophagitis
For the long-term management of patients with healed reflux esophagitis the recommended dose is Omeprazole 10 mg once daily. If needed, the dose can be increased to 20-40 mg once daily.
Treatment of symptomatic gastro-oesophageal reflux disease
The recommended dose is Omeprazole 20 mg daily. Patients may respond adequately to 10 mg daily, and therefore individual dose adjustment should be considered.
If symptom control has not been achieved after four weeks treatment with Omeprazole 20 mg daily, further investigation is recommended.
Treatment of Zollinger-Ellison syndrome
In patients with Zollinger-Ellison syndrome the dose should be individually adjusted and treatment continued as long as clinically indicated. The recommended initial dose is Omeprazole 60 mg daily. All patients with severe disease and inadequate response to other therapies have been effectively controlled and more than 90% of the patients maintained on doses of Omeprazole 20-120 mg daily. When dose exceed Omeprazole 80 mg daily, the dose should be divided and given twice daily.
Paediatric population
Children over 1 year of age and ≥ 10 kg
Treatment of reflux esophagitis
Symptomatic treatment of heartburn and acid regurgitation in gastro-oesophageal reflux disease
The posology recommendations are as follows:

Age	Weight	Posology
≥ 1 year of age	10-20 kg	10 mg once daily. The dose can be increased to 20 mg once daily if needed

≥ 2 years of age	> 20 kg	20 mg once daily. The dose can be increased to 40 mg once daily if needed

Reflux esophagitis: The treatment time is 4-8 weeks.
Symptomatic treatment of heartburn and acid regurgitation in gastro-oesophageal 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.
Children and adolescents over 4 years of age
Treatment of duodenal ulcer caused by H. pylori
When selecting appropriate combination therapy, consideration should be given to official national, regional and 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.
The posology recommendations are as follows:

Weight	Posology
15–30 kg	Combination with two antibiotics: Omeprazole 10 mg, amoxicillin 25 mg/kg body weight and clarithromycin 7.5 mg/kg body weight are all administrated together two times daily for one week.
31–40 kg	Combination with two antibiotics: Omeprazole 20 mg, amoxicillin 750 mg and clarithromycin 7.5 mg/kg body weight are all administrated two times daily for one week.
> 40 kg	Combination with two antibiotics: Omeprazole 20 mg, amoxicillin 1 g and clarithromycin 500 mg are all administrated two times daily for one week.

Special population
Renal impairment
Dose adjustment is not needed in patients with impaired renal function (see section 5.2).
Hepatic impairment
In patients with impaired hepatic function a daily dose of 10–20 mg may be sufficient (see section 5.2).
Elderly
Dose adjustment is not needed in the elderly (see section 5.2).

4.4 **Method of administration**
It is recommended to take Omeprazole capsules in the morning, swallowed whole with half a glass of water. The capsules must not be chewed or crushed.
For patients with swallowing difficulties and for children who can drink or swallow semi-solid food
Patients can open the capsule and swallow the contents with half a glass of water or after mixing the contents in a slightly acidic fluid e.g., fruit juice or applesauce, or in non-carbonated water. Patients should be advised that the dispersion should be taken immediately (or within 30 minutes).
Alternatively patients can suck the capsule and swallow the pellets with half a glass of water. The enteric-coated pellets must not be chewed.

4.5 Contraindications
Hypersensitivity to the active substance(s), substituted benzimidazoles or to any of the excipients listed in section 6.1.

Omeprazole like other proton pump inhibitors (PPIs) must not be used concomitantly with nelfinavir (see section 4.5).

4.6 Special warnings and precautions for use

In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis.

Co-administration of atazanavir with proton pump inhibitors is not recommended (see section 4.5). If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; omeprazole 20 mg should not be exceeded.

Omeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B_{12} (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B_{12} absorption on long-term therapy.

Omeprazole is a CYP2C19 inhibitor. When starting or ending treatment with omeprazole, the potential for interactions with drugs metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and omeprazole (see section 4.5). The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of omeprazole and clopidogrel should be discouraged.

4.7 Interaction with other medicinal products and other forms of interaction

Effects of omeprazole on the pharmacokinetics of other active substances

Active substances with pH dependent absorption

The decreased intragastric acidity during treatment with omeprazole might increase or decrease the absorption of active substances with a gastric pH dependent absorption.

Nelfinavir, atazanavir

The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole.

Concomitant administration of omeprazole with nelfinavir is contraindicated (see section 4.3).

Co-administration of omeprazole (40 mg once daily) reduced mean nelfinavir exposure by ca. 40% and the mean exposure of the pharmacologically active metabolite M8 was reduced by ca. 75 –90%. The interaction may also involve CYP2C19 inhibition.

Concomitant administration of omeprazole with atazanavir is not recommended (see section 4.4). Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10%. Digoxin toxicity has been rarely reported. However caution should be exercised when omeprazole is given at high doses in elderly patients. Therapeutic drug monitoring of digoxin should be then be reinforced.

Clopidogrel

Results from studies in healthy subjects have shown a pharmacokinetic (PK)/pharmacodynamic (PD) interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and omeprazole (80 mg p.o. daily) resulting in a decreased exposure to the active metabolite of clopidogrel by an average of 46% and a decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 16%.

Inconsistent data on the clinical implications of a PK/PD interaction of omeprazole in terms of major cardiovascular events have been reported from both observational and clinical studies. As

a precaution, concomitant use of omeprazole and clopidogrel should be discouraged (see section 4.4).

Other active substances
The absorption of posaconazole, erlotinib, ketoconazole and itraconazole is significantly reduced and thus clinical efficacy may be impaired. For posaconazole and erlotinib concomitant use should be avoided.

4.8 Pregnancy and Lactation

Pregnancy
Results from three prospective epidemiological studies (more than 1000 exposed outcomes) indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Omeprazole can be used during pregnancy.

Breastfeeding
Omeprazole is excreted in breast milk but is not likely to influence the child when therapeutic doses are used.

Fertility
Animal studies with the racemic mixture omeprazole, given by oral administration do not indicate effects with respect to fertility.

4.9 Effects on ability to drive and use machines
Omeprazole is not likely to affect the ability to drive or use machines. Adverse drug reactions such as dizziness and visual disturbances may occur (see section 4.8). If affected, patients should not drive or operate machinery.

5.0 Undesirable effects
The most common side effects (1-10% of patients) are headache, abdominal pain, constipation, diarrhoea, flatulence and nausea/vomiting.

5.1 Overdose
There is limited information available on the effects of overdoses of omeprazole in humans. In the literature, doses of up to 560 mg have been described, and occasional reports have been received when single oral doses have reached up to 2,400 mg omeprazole (120 times the usual recommended clinical dose). Nausea, vomiting, dizziness, abdominal pain, diarrhoea and headache have been reported. Also apathy, depression and confusion have been described in single cases.

The symptoms described have been transient, and no serious outcome has been reported. The rate of elimination was unchanged (first order kinetics) with increased doses. Treatment, if needed, is symptomatic.

6.0 PHARMACOLOGICAL PROPERTIES

6.1 Pharmacodynamics properties

Pharmacotherapeutic group: Drugs for acid-related disorders, proton pump inhibitors, ATC code: A02BC01

6.2 Mechanism of action
Omeprazole, a racemic mixture of two enantiomers reduces gastric acid secretion through a highly targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. It is rapidly acting and provides control through reversible inhibition of gastric acid secretion with once daily dosing.

Omeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the intracellular canaliculi within the parietal cell, where it inhibits the enzyme H+K+-ATPase - the acid pump. This effect on the final step of the gastric acid formation process is dose-dependent and provides for highly effective inhibition of both basal acid secretion and stimulated acid secretion, irrespective of stimulus.

6.3 Pharmacodynamic effects

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

6.4 Pharmacokinetic properties
6.4.1 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%.

6.4.2 Distribution
The apparent volume of distribution in healthy subjects is approximately 0.3 l/kg body weight.

Omeprazole is 97% plasma protein bound.

6.4.3 Elimination
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.

6.5 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 H2-receptor antagonists, proton pump inhibitors and after partial fundectomy. Thus, these changes are not from a direct effect of any individual active substance.

7 PHARMACEUTICAL PARTICULARS

7.1 List of excipients

S/NO	INGREDIENTS	QUANTITY/Batch (KG)
1.	Lactose	18kg
2.	Corn starch	53kg
3.	Methyl paraben	0.28kg
4.	Propyl paraben	0.056kg
5.	Tartrazine yellow	1.0kg
6.	Talc	3kg
7.	Magnesium stearate	2kg
8.	Sodium starch glycolate	2kg
9.	Aerosil	0.8kg

7.2 Incompatibilities
unknown

7.3 Shelf-life
36 months

7.4 Special precautions for storage
Do not store above 30^{oC}. Store in a dry place.

7.5 Nature and composition of immediate packaging
Blisters of 1x14 capsules with EGMP written on the foil on one side and plain PVC on the other..

7.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials
None.

7.0 APPLICANT/MANUFACTURER

7.1 Name and Address
EVERGREEN MORNING STAR PHARMACEUTICALS INDUSTRY LIMITED
NDIOWERRE ORLU L.G.A
ORLU, IMO STATE

7.2 Tel number
+234 703 872 9291
+234 813 693 3443
+234 803 364 9955

7.3 Email
egmpsecdept@gmail.com