1. NAME OF THE MEDICINAL PRODUCT

Omebet (Omeprazole USP 20 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Sr. No.	Ingredients	Actual Qty/Capsule (mg)	Function
Active			
1	Omeprazole USP *(As Enteric Coated Pellets 7.5 % w/w)	266.670	Anti- Ulcerant
Total weight of filled Pellets		**266.670 mg**	
2	Caramel/Pink size '2' hard gelatin capsules IH	1 Nos.	Capsule Shell

3. PHARMACEUTICAL DOSAGE FORMS:

Hard Gelatin Capsule

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

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 oesophagitis
• Long-term management of patients with healed reflux oesophagitis
• Treatment of symptomatic gastro-oesophageal reflux disease
• Treatment of Zollinger-Ellison syndrome Paediatric use

Children over 1 year of age and ≥ 10 kg

• Treatment of reflux oesophagitis
• 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

Route of Administration: oral ***Treatment of duodenal ulcers***

The recommended dose in patients with an active duodenal ulcer is 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 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 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 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 40 mg once daily is recommended and healing is usually achieved within eight weeks
Treatment of NSAID-associated gastric and duodenal ulcers
For the treatment of NSAID-associated gastric and duodenal ulcers, the recommended dose is 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.
Treatment of reflux oesophagitis
The recommended dose is 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 oesophagitis 40 mg once daily is recommended and healing is usually achieved within eight weeks
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 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 20-120 mg daily. When dose exceed 80 mg daily, the dose should be divided and given twice daily.

4.3 Contraindications
Omeprazole is contraindicated in Hypersensitivity to omeprazole, substituted benzimidazoles or to any of the excipients.
4.4 Special warning and precaution for use

4.5 Paediatric population
Not applicable
4.6 Interaction with other medicinal products and other forms of interactions
Omeprazole
Digoxin: Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10%.
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%.
Saquinavir: Concomitant administration of omeprazole with saquinavir/ritonavir resulted in increased plasma levels up to approximately 70% for saquinavir associated with good tolerability in HIV-infected patients.
Tacrolimus: Concomitant administration of omeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.

Methotrexate: When given together with proton-pump inhibitors, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of omeprazole may need to be considered

4.7 Additional information on special populations

Not Applicable

4.8 Paediatric population

Not applicable

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4.9 Fertility, pregnancy and lactation Omeprazole

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.

4.10 Effects on ability to drive and use machines

No influence on the ability to drive and use machines.

4.11 Undesirable effects

Less commonly: blurred vision, pyrexia, anorexia, malaise, chest pain, weight gain, hypoglycaemia, tinnitus, peripheral oedema, neck pain; rarely cholestasis, Stevens- Johnson syndrome, toxic epidermal necrolysis.

Very rarely: hepatitis and jaundice, pancreatitis and hepatic failure. Gastro-intestinal disturbances,

Sleep disturbance, headache, dizziness, depression, paraesthesia, asthenia, peripheral neuropathy, amnesia, fatigue, sexual dysfunction, thrombocytopenia, arthralgia, visual disturbance, alopecia, and hypersensitivity reactions (including rash, pruritus, urticaria, and very rarely lupus erythematosus-like reactions).

4.12 Overdose and Treatments

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

5. Pharmacological properties

5.1 Pharmacodynamic Properties

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

Mechanism of action:

Omeprazole

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.

5.2 Pharmacokinetic Properties

Absorption

Omeprazole and omeprazole magnesium are acid labile and are therefore administered orally as enteric-coated granules in capsules or enteric coated 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.

Biotransformation

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.

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.

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

Hard gelatin capsule Size 2

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

36 months from the date of manufacturing

6.4 Special precautions for storage

Store at a temperature not exceeding 30ºC in a dry place. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

Packing: 2 X 7 Capsule in Alu-Alu Blister Pack

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder and manufacturing site addresses
STALLION LABORATORIES PVT. LTD.
C-1B 305/2, 3, 4& 5 G.I.D.C. KERALA (BAVLA), DIST. AHMEDABAD, GUJARAT, INDIA.