1.6.1 Prescribing information (Summary of products characteristics)

1. Name of the Finished Pharmaceutical Product

1.1 Product name:
SOMECID
(OMEPRAZOLE FOR INJECTION 40 MG)

1.2 Strength:
Each vial contains:
Omeprazole Sodium BP (Lyophilized)
Eq. to Omeprazole 40 mg

1.3 Pharmaceutical dosage forms:
Sterile Dry Powder for injection or infusion

2. Qualitative and Quantitative composition:

Sr. No.	Ingredients	Label Claim (mg)	Actual Qty/ Vial (mg)	Actual Qty/batch (kg)	Function
Active					
1.	Omeprazole Sodium BP *	40.00	124.000	12.400	Proton Pump Inhibitor
Average weight of filled powder			**124.000**	**12.400**	

Inactive Substance: Product is sterile lyophilized powder for injection. Does not contains any added Excipients.

* Quantity to be calculated on the basis of its potency.

Calculation:

Omeprazole Sodium BP Eq. to Omeprazole 40 mg (36.050 % potency)

$$= \frac{\text{Label claim} \times 100 \times \text{Mol wt of Omeprazole Sodium}}{\text{Potency} \times \text{Mol wt of Omeprazole}}$$

$$= \frac{40 \times 100 \times 385.4}{36.050 \times 345.4}$$

= 124 mg/vial

3. Pharmaceutical forms

A White or almost white lyophilized powder, hygroscopic.

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

4.2 Posology and Method of administration

Alternative to oral therapy
In patients where the use of oral medicinal products is inappropriate, Somecid once daily is recommended. In patients with Zollinger-Ellison Syndrome the recommended initial dose of Somecid given intravenously is 60 mg daily. Higher daily doses may be required and the dose should be adjusted individually. When doses exceed 60 mg daily, the dose should be divided and given twice daily.
Somecid solution for injection must be given only as an intravenous injection and it must not be added to infusion solutions. After reconstitution the injection should be given slowly over a period of at least 2.5 minutes at a maximum rate of 4 ml per minute.

Special populations
Impaired renal function
Dose adjustment is not needed in patients with impaired renal function.
Impaired hepatic function
In patients with impaired hepatic function a daily dose of 10-20 mg may be sufficient
Elderly (> 65 years old)
Dose adjustment is not needed in the elderly
Paediatric patients
There is limited experience with Somecid for intravenous use in children.

4.3 Method of administration

Intravenous

4.4 Contraindications

Hypersensitivity to Omeprazole, substituted benzimidazole or to any of the excipients.
Omeprazole like other proton pump inhibitors (PPIs) should not be used concomitantly with nelfinavir

4.5 Special warning and precaution for use

In the presence of any alarm symptoms (eg, 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. 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 B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12absorption on long-term therapy.

4.6 Paediatric population

Omeprazole is not recommended for use in children below 12 years of age because of limited data on safety and efficacy in the age group.

4.7 Interaction with other medicinal products and other forms of interactions

Nelfinavir, atazanavir
The plasma levels of nelfinavir and atazanavir are decreased in case of co-administration with omeprazole.
Digoxin
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.
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%.
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 Additional information on special populations

Not Available

4.9 Paediatric population

Omeprazole is not recommended for use in children below 12 years of age because of limited data on safety and efficacy in the age group.

4.10 Fertility, 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 fetus /newborn child. Omeprazole can be used during pregnancy.

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

4.11 Effects on ability to drive and use machines

omeprazole has no or negligible influence on the ability to drive and use machines.
Adverse drug reactions, such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machines.

4.12 Undesirable effects

- The most common side effects (1-10% of patients) are headache, abdominal pain, constipation, diarrhoea, flatulence and nausea/vomiting.
- Irreversible visual impairment has been reported in isolated cases of critically ill patients who have received omeprazole intravenous injection, especially at high doses, but no causal relationship has been established.

4.13 Overdose

There is limited information available on the effects of overdoses of omeprazole in humans. Nausea, vomiting, dizziness, abdominal pain, diarrhoea and headache have been reported occasionally, and no serious outcome has been reported.
Intravenous doses of up to 270 mg on a single day and up to 650 mg over a three-day period have been given in clinical trials without any dose-related adverse reactions.

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
Intravenous omeprazole produces a dose dependent inhibition of gastric acid secretion in humans. In order to immediately achieve a similar reduction of intragastric acidity as after repeated dosing with 20 mg orally, a first dose of 40 mg intravenously is recommended. This results in an immediate decrease in intragastric acidity and a mean decrease over 24 hours of approximately 90% for both IV injection and IV infusion.
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.
Eradication of H. pylori with omeprazole and antimicrobials is associated with high rates of healing and long-term remission of peptic ulcers.
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.

ATC code- A02BC01

5.2 Pharmacokinetic Properties

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
Total plasma clearance is about 30-40 l/h after a single dose. The plasma elimination half-life of omeprazole is usually shorter than one hour both after single and repeated once-daily dosing. Omeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration. Almost 80% of a 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.

Special populations
Impaired hepatic function
The metabolism of omeprazole in patients with liver dysfunction is impaired, resulting in an increased AUC. Omeprazole has not shown any tendency to accumulate with once-daily dosing.

Impaired renal function
The pharmacokinetics of omeprazole, including systemic bioavailability and elimination rate, are unchanged in patients with reduced renal function.

Elderly
The metabolism rate of omeprazole is somewhat reduced in elderly subjects (75-79 years of age).

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 H2-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

None

6.2 Incompatibilities

None known.

6.3 Shelf Life

24 months from the date of manufacturing

6.4 Special precautions for storage

Store at a temperature not exceeding 30˚C in dry place, Protected from light. Keep out of reach of children.

6.5 Nature and contents of container

Primary Packing: 10 ml Amber coloured Glass Vial.

Secondary Packing: Such 1 Vial is packed in printed carton along with package insert.

6.6 Special precautions for disposal and other handling

None

7. Marketing authorisation holder and manufacturing site addresses

STALLION LABORATORIES PVT.LTD.
817, 8TH FLOOR, DEVPATH, OFF C. G. ROAD,
B/H LAL BUNGLOW, NR. SUPERMALL,
AHMEDABAD –380 006,
GUJARAT, INDIA.

8. Marketing authorisation numbers

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9. Date of First Registration/Renewal of the Registration

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10. Date of revision of Text

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11. Dosimetry (If Applicable)

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12. Instructions for Preparation of Radiopharmaceuticals (If Applicable)
