1. NAME OF THE MEDICINAL PRODUCT

SIVOCID 20 mg capsule

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each capsule contains:

Omeprazole BP	
(As enteric coated granules)	: 20 mg
Excipients	: Q.S.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Red/White colored size "2" capsule.

4. Clinical particulars

4.1 Therapeutic indications

- 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 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

Treatment of duodenal ulcers

The recommended dose in patients with an active duodenal ulcer is Omeprazole 20mg once daily. In most patients healing occurs within two 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 20mg once daily

Method of administration: Oral

4.3 Contraindications

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

4.4 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. 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 B12 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. The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of Omeprazole and clopidogrel should be discouraged.
Some children with chronic illnesses may require long-term treatment although it is not recommended.
Hypomagnesaemia
Severe Hypomagnesaemia has been reported in patients treated with PPIs like Omeprazole for at least three months, and in most cases for a year. Serious manifestations of Hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, Hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.
Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as
Salmonella and Campylobacter.

4.5 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.
The co-administration of Omeprazole (20 mg once daily) with atazanavir 400 mg/ritonavir 100 mg to healthy volunteers resulted in a decrease of approximately 30% in the atazanavir exposure as compared to atazanavir 300 mg/ritonavir 100 mg once daily.

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. 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

In a crossover clinical study, clopidogrel (300 mg loading dose followed by 75 mg/day) alone and with Omeprazole (80 mg at the same time as clopidogrel) were administered for 5 days. The exposure to the active metabolite of clopidogrel was decreased by 46% (Day 1) and 42% (Day 5) when clopidogrel and Omeprazole were administered together. Mean inhibition of platelet aggregation (IPA) was diminished by 47% (24 hours) and 30% (Day 5) when clopidogrel and Omeprazole were administered together.

Phenytoin

Monitoring phenytoin plasma concentration is recommended during the first two weeks after initiating Omeprazole treatment and, if a phenytoin dose adjustment is made, monitoring and a further dose adjustment should occur upon ending Omeprazole treatment.

4.6 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.

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

Fertility: No data available

4.7 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

4.8 Undesirable effects

The following adverse drug reactions have been identified or suspected in the clinical trials programme for Omeprazole and post-marketing. None was found to be dose-related. Adverse reactions listed below are classified according to frequency and System Organ Class (SOC). Frequency categories are defined according to the following convention:
Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), Not known (cannot be estimated from the available data).

Blood and lymphatic system disorders
Rare: Leukopenia, thrombocytopenia
Very rare: Agranulocytosis, pancytopenia
Immune system disorders
Rare: Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock
Metabolism and nutrition disorders
Rare: Hyponatraemia
Not Known: Hypomagnesaemia
Psychiatric disorders
Uncommon: Insomnia
Rare: Agitation, confusion, depression
Very rare: Aggression, hallucinations
Nervous system disorders
Common: Headache
Uncommon: Dizziness, paraesthesia, somnolence
Rare Taste disturbance
Eye disorders
Rare: Blurred vision
Ear and labyrinth disorders
Uncommon: Vertigo
Respiratory, thoracic and mediastinal disorders
Rare: Bronchospasm
Gastrointestinal disorders
Common: Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting, Fundic gland polyps (benign)
Rare: Dry mouth, stomatitis, gastrointestinal candidiasis
Not Known: microscopic colitis
Hepatobiliary disorders
Uncommon: Increased liver enzymes
Rare: Hepatitis with or without jaundice
Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease
Skin and subcutaneous tissue disorders
Uncommon: Dermatitis, pruritus, rash, urticaria
Rare: Alopecia, photosensitivity
Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN)
Not known: Subacute cutaneous lupus erythematosus
Musculoskeletal and connective tissue disorders
Uncommon: Fracture of the hip, wrist or spine

Rare: Arthralgia, myalgia
Very rare: Muscular weakness
Renal and urinary disorders
Rare: Interstitial nephritis
Reproductive system and breast disorders
Very rare: Gynaecomastia
General disorders and administration site conditions
Uncommon: Malaise, peripheral oedema
Rare: Increased sweating

4.9 Overdose

Symptoms of 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, diarrhea and headache have been reported. Also apathy, depression and confusion have been described in single cases.

Treatment of overdose:

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 Pharmacodynamics properties

Pharmacotherapeutic group: Selective proton plump inhibitor, substituted benzimidazole

ATC Code: A02B C01

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.

5.2 Pharmacokinetic properties

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

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 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

Placebo pellets	IHS	13.33 mg
Red/White capsule size "2"	IHS	1 Nos.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store below 30°C. Protect from light, and moisture.
KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container<and special equipment for use, administration or implantation>

2 X 7 Capsules of Alu/Alu is packed in a carton with package insert.

6.6 Special precautions for disposal <and other handling>

No special requirements.

7. APPLICANT/MANUFACTURER

Ahmedabad
Email : info@sagalabs.com
URL : www.sagalabs.com