SUMMARY OF PRODUCT CHARACTERISTICS

HELIFAS H.PYLORI KIT

(A Combikit of Amoxicillin capsules BP, Clarithromycin Tablets USP & Esomeprazole Magnesium Delayed-Release Capsules USP)

1. NAME OF THE MEDICINAL PRODUCT

A Combikit of Amoxicillin capsules BP, Clarithromycin Tablets USP & Esomeprazole Magnesium Delayed-Release Capsules USP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Combikit Contains:

A. Amoxicillin capsules BP 500 mg (2 Capsules)

Each capsule contains:

Amoxicillin Trihydrate BP

Equivalent to Amoxicillin 500 mg

Excipients q.s.

Approved colour used in hard gelatin capsule shells

B. Clarithromycin Tablets USP (1 Tablet)

Each film coated tablet contains:

Clarithromycin USP 500 mg

Excipients q.s.

Colour: Brilliant blue Lake & Titanium Dioxide USP

C. Esomeprazole Magnesium Delayed-Release Capsules USP (1 Capsule)

Each capsule contains:

Esomeprazole Magnesium USP

Equivalent to Esomeprazole 20 mg

Approved colour used in hard gelatin capsule shells

3. PHARMACEUTICAL FORM

A Combi-kit of Capsules & Tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Amoxicillin-Penicillin like antibiotics

Clarithromycin-Macrolide antibiotics

Esomeprazole-Proton pump inhibitors

HP KIT are indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) to eradicate H. pylori. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence.

4.2 Dosage and Administration

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence. The recommended adult oral dose is one strip of **HELIFAS H.PYLORI KIT** (20 mg Esomeprazole, 500 mg Amoxicillin, and 500 mg clarithromycin) administered twice daily (morning and evening) for 10 or 14 days (see INDICATIONS).

HELIFAS H.PYLORI KIT is not recommended in patients with creatinine clearance less than 30 mL per min.

Mode of administration

Oral

4.3 Contraindications

HELIFAS H.PYLORI KIT contraindicated in patients with known hypersensitivity to any component of the formulation of esomeprazole.

A history of allergic reaction to any of the penicillin's is a contraindication.

Concomitant administration of **HELIFAS H.PYLORI KIT** and any of the drugs is contraindicated like cisapride, pimozide, astemizole, terfenadine, ergotamine or dihydroergotamine.

4.4 Warnings and Precautions

Amoxicillin

- Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillin's, cephalosporins, or other allergens.
- Erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.
- Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

Clarithromycin

- Liver function impairment
- Renal function impairment (severe)
- Rhabdomyolysis has been reported with concomitant use of Clarithromycin and HMG CoA reductase inhibitors.
- Rifabutin and rifampicin May decrease serum concentration of Clarithromycin by >50%.
- Theophylline - The area under the plasma concentration-time curve is increased.

Esomeprazole

- It is advisable for patients to seek medical advice if:
- Loss of significant and unintentional weight, recurrent vomiting, dysphagia, haematemesis or melena and in case of suspicion of occurrence of gastric ulcer, the possibility of malignancy should be excluded, as treatment with esomeprazole may alleviate symptoms and delay diagnosis.
- Gastric ulcer or gastrointestinal surgery.

4.5 Drug Interactions

Amoxicillin

- Probenecid may decrease the renal tubular secretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.
- Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.
- Excretion of methotrexate is reduced by penicillin's; increased risk of toxicity.
- The oral typhoid vaccine is inactivated by antibacterial.

Clarithromycin

- Serious adverse reactions have been reported in patients taking clarithromycin concomitantly with CYP3A4 substrates. These include colchicine toxicity with colchicine; rhabdomyolysis with simvastatin, lovastatin, and atorvastatin; and hypotension with calcium channel blockers metabolized by CYP3A4 (e.g., verapamil, amlodipine, diltiazem).

Esomeprazole

- The serum concentration of Acenocoumarol can be increased when it is combined with Esomeprazole.
- The metabolism of Adinazolam, Almotriptan, Ambrisentan, Aminophenazone, Amiodarone, Amitriptyline, can be decreased when combined with Esomeprazole.

4.6 Pregnancy and Lactation

Amoxicillin: The product should only be used during pregnancy where potential benefits outweigh the potential risks associated with treatment. Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the breast-fed infant.

Clarithromycin: Safety and efficacy in pregnancy and lactation have not been established. Clarithromycin is excreted in the breast milk.

Esomeprazole: Caution should be exercised when prescribing to pregnant and breast-feeding women.

4.7 Effects on Ability to Drive and Use Machines

None

4.8 Adverse Effects

Acute ingestion of large doses of amoxicillin may cause nausea, vomiting, diarrhoea and abdominal pain. Acute oliguric renal failure and haematuria may occur in large doses.

Symptoms of toxicity of clarithromycin include diarrhea, nausea, abnormal taste, dyspepsia, and abdominal discomfort. Transient hearing loss with high doses has been observed. Pseudomembranous colitis has been reported with clarithromycin use.

4.9 Overdosage

Amoxicillin: Gastrointestinal effects such as nausea, vomiting and diarrhea may be evident and should be treated symptomatically with attention to the water/electrolyte balance.

Clarithromycin: Over dosage of clarithromycin can cause gastrointestinal symptoms such as abdominal pain, vomiting, nausea, and diarrhea.

Esomeprazole: The symptoms described in connection with 280 mg were gastrointestinal symptoms and weakness. Single doses of 80 mg esomeprazole were uneventful. Treatment should be symptomatic and general supportive measures should be utilized.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Amoxicillin: J01CA04

Clarithromycin: J01FA09

Esomeprazole: A02BC05

Amoxicillin: Amoxicillin competitively inhibit penicillin binding proteins, leading to upregulation of autolytic enzymes and inhibition of cell wall synthesis. Amoxicillin has a long duration of action as it is usually given twice daily. Amoxicillin has a wide therapeutic range as mild overdoses are not associated with significant toxicity. Patients should be counselled regarding the risk of anaphylaxis, Clostridium difficile infections, and bacterial resistance.

Clarithromycin: Clarithromycin is a macrolide antibiotic whose spectrum of activity includes many gram-positive (Staphylococcus aureus, S. pneumoniae, and S. pyogenes) and gram-negative aerobic bacteria (Haemophilus influenza, H. parainfluenza, and Moraxella catarrhalis), many anaerobic bacteria, some mycobacteria, and some other organisms including Mycoplasma, Ureaplasma, Chlamydia, Toxoplasma, and Borrelia. Other aerobic bacteria that clarithromycin has activity against include C. pneumoniae and M. pneumoniae. Clarithromycin has an in-vitro activity that is similar or greater than that of erythromycin against erythromycin-susceptible organisms. Clarithromycin is usually bacteriostatic, but may be bactericidal depending on the organism and the drug concentration.

Esomeprazole: Esomeprazole is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing of erosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcer recurrence. Esomeprazole belongs to a new class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonistic properties, but that suppress gastric acid secretion by specific inhibition of the H+/K+ ATPase at the secretory surface of the gastric parietal cell. By doing so, it inhibits acid secretion into the gastric lumen. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

5.2 Pharmacokinetic properties

Amoxicillin Capsules: Amoxicillin is semi-synthetic, broad-spectrum penicillin Amoxicillin is rapidly absorbed after oral administration and provides high blood levels and very high concentrations in the tissues and urine. Amoxicillin does not appear to be metabolized in the

body. Urinary excretion is rapid, and only unchanged amoxicillin is recovered in the urine. Approximately 17% of amoxicillin is bound by serum proteins. Amoxicillin is particularly effective in-vitro against the following organisms; Gram-positive cocci, Strep. agalactiae, Strep. faecalis, Strep. Pneumoniae and penicillin-sensitive N. gonorrhoea, Gram-negative bacilli, Listeria monocytogenes.

Clarithromycin: Clarithromycin is absorbed rapidly from the gastrointestinal tract after oral administration, but its bioavailability is reduced to 50 to 55% because of rapid first-pass metabolism. Clarithromycin may be given with or without food. Protein binding of Clarithromycin ranges from 40 to 70% and is concentration-dependent. The elimination half-life of clarithromycin and 14-hydroxyclarithromycin are approximately 3 to 7 and 5 to 9 hours respectively. Clarithromycin is eliminated by renal and nonrenal routes. The amount of clarithromycin excreted unchanged in the urine ranges from 20 to 40%.

Esomeprazole Magnesium: Esomeprazole belongs to a new class of anti-secretory compounds. Esomeprazole is a compound that inhibits gastric acid secretion and is indicated in the treatment of gastroesophageal reflux disease (GERD), the healing of erosive esophagitis, and H. pylori eradication to reduce the risk of duodenal ulcer recurrence. Absorption of oral administration is 90%, volume of distribution is 16L, and protein binding is 97%, metabolism by hepatic. Esomeprazole is completely metabolized by the cytochrome P450 system via CYP2C19 and CYP3A4. Less than 1% of the parent drug is excreted in urine. Approximately 80% of the administered dose of esomeprazole is excreted as metabolites in urine and the remaining 20% is excreted in feces. Half Life is 1-1.5 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Amoxicillin Trihydrate Capsules

Magnesium Stearate, Purified talc, Colloidal Silicon Dioxide, Capsule Shell ‘O’.

Clarithromycin Tablets USP

Microcrystalline cellulose (Ph-101), Lactose, Sodium Starch Glycolate, Corn starch, Purified water, Poly vinyl Pyrolidone k-30, Magnesium Stearate, Talc, Colloidal Silicon Dioxde, Sodium Lauryl Sulphate, Croscarmellose Sodium(Ac-di Sol), Hypermellose (Hydroxy propyl methyl cellulose), Titanium Dioxide, Talc, Polyethylene Glycol 6000, Isopropyl alcohol, Methylene Chloride, Colour: Brilliant blue Lake.

Esomeprazole:

Capsule shells‘2’ Colour Pink/Clear (Hard Gelatin Capsules Shells)

6.2 Incompatibilities

Not known

6.3 Shelf Life

36 months from the date of manufacturing.

6.4 Storage Conditions

Store below 30°C. Protect from light and moisture.

6.5 Nature and content of container

2 Strips (One Kit) packed in printed one inner carton with package insert and such 7 inner printed cartons packed in one outer printed carton.

One Alu/Pvc strip contains 2 Amoxicillin Capsules, 1 Clarithromycin Tablets & 1 Esomeprazole Magnesium Delayed-Release Capsules.

7. MARKETING AUTHORIZATION HOLDER

BLISS GVS PHARMA LTD

102, Hyde Park, Saki vihar Road, Andheri (east),

Mumbai – 400 072, India.