Summary of Product Characteristics

1. Name of the Medicinal Product
Europyl Kit (H. Pylori Kit)

2. Qualitative & Quantitative Composition:
Each hard gelatin capsule contains;
Lansoprazole 30mg

Each film-coated tablet contains;
Tinidazol BP.....500mg

Each film-coated tablet contains;
Clarithromycin USP.....500mg

For full list of excipients, see section 6.1 of SmPC

3. Pharmaceutical Form:
KIT (Capsules & Tablet)

Visual Description
Lansoprazole Capsules: Red cap/Clear transparent coloured body hard gelatin '1' size capsule containing a white coloured enteric coated granules.
Tinidazole Tablets: Yellow coloured, oblong shaped, biconvex film coated tablets.
Clarithromycin Tablets: Yellow coloured, elongated oblong shaped slightly biconvex film coated tablets having break-lines on one side.

4. Clinical Particulars
4.1 Therapeutic Indications:
Europyl Kit is indicated for the eradication of *H. pylori* in active chronic gastritis, duodenal and gastric ulcers.

4.2 Posology and Method of Administration:
One Europyl Kit pack contains two capsules of lansoprazole (30 mg), two tablets of tinidazole (500 mg) and two tablets of clarithromycin (250 mg). One pack is for one day treatment. From this specially designed pack, one capsule of lansoprazole, one tablet of tinidazole and one tablet of clarithromycin is to be taken in the morning and similarly one each in the evening. The duration of therapy recommended is for seven days.
Renal and Hepatic impairment: Caution should be exercised while administering Europyl Kit with renal impairment and hepatic disease.
The red portion of strip indicates morning dosage to be taken before breakfast. It contains:
1 Capsule (Lansoprazole)
1 Dark Yellow tablet (Tinidazole)
1 Light Yellow tablet (Clarithromycin)
The Blue portion of strip indicates evening dosage to be taken before dinner. It contains:
1 Capsule (Lansoprazole)

1 Dark Yellow tablet (Tinidazole)
1 Light Yellow tablet (Clarithromycin)

4.3 Contraindications:
Europyl Kit is contraindicated to patients hypersensitive to lansoprazole or tinidazole or clarithromycin or to any other ingredients in the formulation.

4.4 Special warnings and precautions for use
Pseudomembranous colitis has occurred with nearly all antibacterial agents including clarithromycin and may range in severity from mild to life-threatening. Therefore it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of Europyl Kit.

4.5 Interactions with other medicinal products and other forms of Interactions
Theophylline - Clarithromycin use in patients who are receiving theophylline may be associated with an increase in serum theophylline concentrations.
Carbamazepine - Concomitant administration of single doses of clarithromycin and carbamazepine has been shown to result in increased plasma concentrations of carbamazepine.
Warfarin - The use of clarithromycin in patients receiving warfarin may result in potentiation of the effects of warfarin. Prothrombin time should be frequently monitoredin these patients.
Digoxin -The effects of digoxin may be potentiated with concomitant administration ofclarithromycin.
T*erfenadine* - Concomitant administration of single dose of clarithromycin and terfenadine have been shown to result in increased plasma concentrations of terfenadine.Clarithromycin should not be given to patients receiving terfenadine therapy who have pre-existing cardiac abnormalities (arrhythmia, bradycardia, QT interval prolongation, ischemic heart disease, congestive heart failure) or electrolyte disturbances.
*Ergo*t - The theoretical possibility of ergotism contraindicates the concurrent use of clarithromycin with ergot derivatives.
Cyclosporin - Clarithromycin increases the serum concentration of cyclosporin hence thedosage of latter may be reduced to avoid renal toxicity.
The use of clarithromycin in patients concurrently taking drugs metabolised by the cytochrome P450 system may be associated with elevations in serum levels of these drugs.
Ketoconazole, Ampicillin esters, Iron salts - Lansoprazole causes a profound and long lasting inhibition of gastric acid secretion. Therefore it is possible that lansoprazole may interfere with the absorption of these drugs.
Alcohol - Intake of alcohol during this therapy can precipitate an antabuse effect and hence should be avoided.
Disulfiram - Concomitant administration can cause delirium and confusion.

4.6 Pregnancy and Lactation
Pregnancy
Lansoprazole, Tinidazole, Clarithromycin: There are no well controlled studies of lansoprazole or tinidazole or clarithromycin in pregnant women. Clarithromycin is not indicated during pregnancy, Clarithromycin has demonstrated adverse effects of pregnancy outcome and embryo-foetal development in monkeys, rats, mice, and rabbits at doses that produced plasma levels 2 to 17 times the serum levels achieved

in humans treated at the maximum recommended human doses.Hence this combination is not indicated in pregnancy.

Lactation

It is not known whether lansoprazole or tinidazole or clarithromycin is excreted in breast milk. Caution should be exercised when administering to a nursing woman.

Paediatric Use

Safety and effectiveness of Europyl Kit in pediatric population has not been established.

4.7 Effects on ability to drive and use machine*:

Not Known.

4.8 Undesirable Effects*:

The drugs of the Europyl Kit are well tolerated. Side effects include nausea, vomiting, diarrhoea and abdominal pain. Other rare side effects include headache, skin rash, metallic taste (change in taste), rarely glossitis, stomatitis, urticaria, eruptions and moderate leucopenia.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose:

In case of overdosage, discontinue medication, treat symptomatically, and institute supportive measures as required.

5. Pharmacological properties:

5.1 Pharmacodynamic Properties:

Lansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H+, K+) -ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, Lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus. Lansoprazole does not exhibit anticholinergic or histamine type-2 antagonist activity.

Tinidazole is an antiprotozoal, antibacterial agent. The nitro- group of Tinidazole is reduced by cell extracts of Trichomonas. The free nitro- radical generated as a result of this reduction may be responsible for the antiprotozoal activity. Chemically reduced Tinidazole was shown to release nitrites and cause damage to purified bacterial DNA in vitro. Additionally, the drug caused DNA-base changes in bacterial cells and DNA strandbreakage in mammalian cells. The mechanism by which Tinidazole exhibits activityagainst Giardia and Entamoeba species is not known.

Clarithromycin is a macrolide antibiotic. Clarithromycin exerts its antibacterial action by binding to the 50 S ribosomal subunits of susceptible bacteria and suppresses protein synthesis. The 14-OH metabolite of Clarithromycin is twice as active as the parent compound against certain organisms.

Clarithromycin has demonstrated excellent in vitro activity against both standard strains of bacteria and clinical isolates. It is highly potent against a wide variety of aerobic and anaerobic Gram-positive and Gram-negative organisms. The minimum inhibitory concentrations (MIC) of Clarithromycin are generally one log2 dilution more

potent than the MICs of erythromycin. In vitro data also indicate clarithromycin has excellent activity against Legionella pneumophila, Mycoplasma pneumoniae, and Helicobacter (Campylobacter) pylori. In vitro and in vivo data show that this antibiotic has significant activity against clinically significant mycobacterial species. The in vitro data indicate enterobacteriaceae, pseudomonas species and other non-lactose fermenting gram negativebacilli are not sensitive to Clarithromycin. Clarithromycin is bactericidal to Helicobacter pylori, with activity greater at neutral pH than at acid pH.

5.2 Pharmacokinetics Properties*:

Lansoprazole

Absorption - The absorption of lansoprazole is rapid, with mean C max occurring approximately 1.5 to1.7 hours after oral dosing, and relatively complete with absolute Bioavailability over 80%. The mean plasma half-life was 1.5 (±1.0) hours.

Distribution - Lansoprazole is 97% bound to plasma proteins.

Metabolism - Lansoprazole is extensively metabolized in the liver. Two metabolites havebeen identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species, which inhibit acid secretion by (H +, K +) -ATPase within the parietal cell canaliculus, but are not present in the systemic circulation. The plasma elimination half-life of lansoprazole doesnot reflect its duration of suppression of gastric acid secretion. Thus, the plasma elimination half-life is less than 2 hours, while the acid inhibitory effect lasts more than 24 hours.

Elimination - Following single-dose oral administration of lansoprazole, virtually no unchanged lansoprazole was excreted in the urine. In one study, after a single oral dose of14 C-lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces.

Tinidazole

Absorption - Rapid and complete after oral administration. C max is 47.7 mcg/mL; T-max is 1.6 h; AUC is 901.6 mcgh/mL at 72 h. Steady-state conditions reached in 2.5 to 3days.

Distribution - Distributed to virtually all tissues and body fluid and crosses the blood brain barrier. Vd is about 50 L. Protein binding is 12%.

M**etabolism** - Partly metabolized by oxidation, hydroxylation, and conjugation. Metabolized by CYP3A4.

Elimination - Plasma t ½ is 12 to 14 h. Elimination t ½ is 13.2 h. About 20% to 25% excreted unchanged in urine and 12% in feces.

Clarithromycin

Absorption - Clarithromycin is absorbed rapidly from the gastro-intestinal tract after oral administration, but its bioavailability is reduced to 50% to 55% because of rapid first-pass metabolism. Peak plasma concentration occurs approximately 2 hours after administration. Clarithromycin may be given with or without food.

Distribution - Both clarithromycin and 14-hydroxyclarithromycin distribute widely throughout the body and achieve high intracellular concentrations. Tissue concentrations generally exceed serum concentrations. Clarithromycin does not achieve significant levels in the cerebrospinal fluid. Protein binding of clarithromycin ranges from 40 to 70% and is concentration-dependent. The elimination half-lives of clarithromycin and 14-hydroxyclarithromycin are approximately 3 to 7 and 5 to 9 hours respectively. Longer half-lives are observed after larger doses.

Metabolism - Clarithromycin is metabolised by the liver to the active metabolite, 14-Hydroxyl clarithromycin, as well as to several other metabolites.
Elimination - Clarithromycin is eliminated by renal and non-renal routes. The amount of clarithromycin excreted unchanged in the urine ranges from 20 to 40%, depending on the dose administered and the formulation. Between 10 and 15% of the dose is excreted in the urine as the 14-hydroxy metabolite.

5.3 Preclinical safety data
None Known.

6. Pharmaceutical particulars:
6.1 List of Excipients:
LANSOPRAZOLE: EHG Capsules "1" size plain Red Transparent/ Clear Transparent capsules IHS 1 NO.

TINIDAZOLE:
Starch BP, Sodium Starch Glycolate BP, Micro Crystalline CelluloseBP, Starch BP, PVK-30/ Povidone BP, Starch BP, Colloidal silicon dioxide BP, Microcrystalline Cellulose powder BP, HPMC E-15/ Methocel BP, Colour -Titanium Dioxide BP, Propylene Glycol BP, Poly Ethylene Glycol BP, Talc (Extra White) BP, Isopropyl Alcohol BP , Colour - Tartrazine Supra FCF IHS

CLARITHROMYCIN
Lactose BP, Starch BP, Microcrystalline Cellulose Powder BP
, PVP K-30/ Povidone BP, Isopropyl Alcohol BP Q.S., Talc BP
, Magnesium Stearate BP, Sodium Starch Glycolate BP,
Starch BP, Purified Water BP Q.s., HPMC E-15/ Methocel BP,
Colour – Titanium Dioxide BP , Colour – Quinoline Yellow WS IHS,
Isopropyl alcohol BP Q.S., Methylene Chloride BP Q.S., Talc BP 8.00 mg, Tween – 80 (Polysorbate) BP, Sodium Starch Glycolate BP, Magnesium Stearate BP, Purified water BP

6.2 Incompatibilities:
Not applicable

6.3 Shelf life:
24 months from the date of manufacture.

6.4 Special Precautions for storage:
Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container:
Mono Carton containing Kit of One Strip having:
2 Lansoprazole Capsules 30 mg
2 Tinidazole Tablets 500 mg
2 Clarithromycin Tablets USP 250 mg
7 such Mono Cartons in one outer carton.
Carton of Seven Kit.

6.6 Special precautions for disposal:
Not applicable.

7. Marketing Authorization Holder:
Sterling Lab
57, Sipcot Industrial Complex Hosur-635126 Tamilnadu, India

8. Marketing Authorization Numbers:
H2022/CTD7381/13205

9. Date of first registration /renewal of the registration:
2022 June 02

10. Date of revision of text:
2022 June 02