## PYLOCIDE KIT

(2 Lansoprazole+2 Tinidazole+2 Clarithromycin)

**COMPOSITION:**

Each Kit Contains:

(A) 2 Lansoprazole Delayed Release capsules USP 30 mg
Each hard gelatin capsule contains:
Lansoprazole USP 30 mg
(as enteric coated pellets)
Excipients q.s.
Approved colour used in empty capsule shells.

(B) 2 Tinidazole Tablets 500 mg
Each film coated tablet contains:
Tinidazole BP 500 mg
Excipients q.s.
Colour : Quinoline Yellow & Titanium Dioxide BP

(C) 2 Clarithromycin tablets USP 250 mg
Each film coated tablet contains :
Clarithromycin USP 250 mg
Excipients q.s.
Colour : Titanium dioxide BP

**PHARMACODYNAMIC:**

**Pharmacotherapeutic group:** Antacids, Antireflux Agents & Antiulcerants

**ATC code:** A02BD

**Mechanism of actions:**

- Killing bacteria and reducing the infection.
- Inhibiting the bacterial growth.
- Decreasing the amount of acid made in the stomach.

**PHARMACOKINETIC:**

**Lansoprazole**

Absorption is rapid, with mean peak plasma levels of lansoprazole occurring after approximately 1.7 hours. After single-dose administration of 15 mg to 60 mg of oral lansoprazole, the peak plasma concentrations (Cmax) of lansoprazole and the area under the plasma concentration curves (AUCs) of lansoprazole were approximately proportional to the administered dose. Lansoprazole does not accumulate and its pharmacokinetics is unaltered by multiple dosing. Absorption The absorption of lansoprazole is rapid, with the mean Cmax occurring approximately 1.7 hours after oral dosing, and the absolute bioavailability is over 80%. In healthy subjects, the mean (±SD) plasma half-life was 1.5 (±1.0) hours. Both the Cmax and AUC are diminished by about 50 to 70% if lansoprazole is given 30 minutes after food, compared with the fasting condition. There is no significant food effect if lansoprazole is given before meals.

Distribution Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0 mcg/mL.

Metabolism Lansoprazole is extensively metabolized in the liver. Two metabolites have been 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 that inhibit acid secretion by blocking the proton pump at the secretory surface of the gastric parietal cell. The two active species are not present in the systemic circulation. The plasma elimination half-life of lansoprazole is less than 2 hours while the acid inhibitory effect lasts more than 24 hours. Therefore, the plasma elimination half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion.

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 of 14C-lansoprazole, approximately onethird of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the lansoprazole metabolites.

**Tinidazole**

Absorption After oral administration, tinidazole is rapidly and completely absorbed. A bioavailability study of tinidazole tablets was conducted in adult healthy volunteers. All subjects received a single oral dose of 2 g (four 500 mg tablets) of tinidazole following an overnight fast. Oral administration of four 500 mg tablets of tinidazole under fasted conditions produced a mean peak plasma concentration (Cmax) of 47.7 (±7.5) mcg/mL, with a mean time to peak concentration (Tmax) of 1.6 (±0.7) hours, and a mean area under the plasma concentration-time curve (AUC0–infinity) of 901.6 (± 126.5) mcg.hr/mL at 72 hours. The elimination half-life (T½) was 13.2 (±1.4) hours. Mean plasma levels decreased to 14.3 mcg/mL at 24 hours, 3.8 mcg/mL at 48 hours, and 0.8 mcg/mL at 72 hours following administration. Steady-state conditions are reached in 2½ to 3 days of multi-day dosing. Administration of tinidazole tablets with food resulted in a delay in the Tmax of approximately 2 hours and a decline in the Cmax of approximately 10%, compared with fasted conditions. However, administration of tinidazole with food did not affect AUC or T½ in this study. In healthy volunteers, administration of crushed tinidazole tablets in artificial cherry syrup, after an overnight fast, had no effect on any pharmacokinetic parameter as compared with tablets swallowed whole under fasted conditions.

Distribution Tinidazole is distributed into virtually all tissues and body fluids, and also crosses the blood-brain barrier. The apparent volume of distribution is about 50 liters. Plasma protein binding of tinidazole is 12%. Tinidazole crosses the placental barrier and is secreted in breast milk.

Metabolism Tinidazole is significantly metabolized in humans prior to excretion. Tinidazole is partly metabolized by oxidation, hydroxylation and conjugation. Tinidazole is the major drug-related constituent in plasma after human treatment, along with a small amount of the 2-hydroxymethyl metabolite. Tinidazole is biotransformed mainly by cytochrome (CY) P3A4. In an in vitro metabolic drug interaction study, tinidazole concentrations of up to 75 mcg/mL did not inhibit the enzyme activities of CYP1A2, CYP2B6, CYP2C9, CYP2D6, CYP2E1, and CYP3A4. The potential of tinidazole to induce the metabolism of other drugs has not been evaluated.

Elimination The plasma half-life of tinidazole is approximately 12 to 14 hours. Tinidazole is excreted by the liver and the kidneys. Tinidazole is excreted in the urine mainly as unchanged drug (approximately 20 to 25% of the administered dose). Approximately 12% of the drug is excreted in the feces.

**Clarithromycin**

Clarithromycin is absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability of 250 mg clarithromycin tablets was approximately 50%. For a single 500 mg dose of clarithromycin, food slightly delays the onset of clarithromycin absorption, increasing the peak time from approximately 2 to 2.5 hours. Food also increases the clarithromycin peak plasma concentration by about 24%, but does not affect the extent of clarithromycin bioavailability. Food does not affect the onset of formation of the antimicrobially active metabolite, 14-OH-clarithromycin or its peak plasma concentration but does slightly decrease the extent of metabolite formation, indicated by an 11% decrease in area under the plasma concentration-time curve (AUC). In non-fasting healthy human subjects (males and females), peak plasma concentrations were attained within 2 to 3 hours after oral dosing. Steady-state peak plasma clarithromycin concentrations were attained within 3 days and were approximately 1 to 2 mcg/mL with a 250 mg dose administered every 12 hours, and 3 to 4 mcg/mL with a 500 mg dose administered every 8 to 12 hours. The elimination half-life of clarithromycin was about 3 to 4 hours with 250 mg administered every 12 hours, but increased to 5 to 7 hours with 500 mg administered every 8 to 12 hours. The nonlinearity of clarithromycin pharmacokinetics is slight at the recommended doses of 250 mg and 500 mg administered every 8 to 12 hours. With a dosing of 250 mg every 12 hours, the principal metabolite, 14-OH-clarithromycin, attains a peak steady-state concentration of about 0.6 mcg/mL and has an elimination half-life of 5 to 6 hours. With a dosing of 500 mg every 8 to 12 hours, the peak steady-state concentration of 14-OH-clarithromycin is slightly higher (up to 1 mcg/mL), and its elimination half-life is about 7 to 9 hours. With any of these dosing regimens, the steady-state concentration of this metabolite is generally attained within 3 to 4 days. After a 250 mg tablet every 12 hours, approximately 20% of the dose is excreted in the urine as clarithromycin, while after a 500 mg tablet every 12 hours, the urinary excretion of clarithromycin is somewhat greater, approximately 30%. In comparison, after an oral dose of 250 mg (125 mg/5 mL) suspension every 12 hours, approximately 40% is excreted in urine as clarithromycin. The renal clearance of clarithromycin is, however, relatively independent of the dose size and approximates the normal glomerular filtration rate. The major metabolite found in urine is 14-OH-clarithromycin, which accounts for an additional 10 to 15% of the dose with either a 250 mg or a 500 mg tablet administered every 12 hours. Steady-state concentrations of clarithromycin and 14-OH-clarithromycin observed following administration of 500 mg doses of clarithromycin every 12 hours to adult patients with HIV infection were similar to those observed in healthy volunteers. In adult HIV-infected patients taking 500 mg or 1,000 mg doses of clarithromycin every 12 hours, the steady-state clarithromycin Cmax values ranged from 2 to 4 mcg/mL and 5 to 10 mcg/mL, respectively.

**INDICATION:**

PYLOCIDE KIT is indicated for the eradication of H. pylori in active chronic gastritis, duodenal and gastric ulcers.

**POSOLOGY AND METHOD OF ADMINISTRATION:**

One PYLOCIDE 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 1 day of 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 7 days.

**SPECIAL WARNING AND PRECAUTION FOR USE:**

Before using PYLOCIDE KIT, inform your doctor about your current list of medications, over the counter products (e.g. vitamins, herbal supplements, etc.), allergies, pre-existing diseases, and current health conditions (e.g. pregnancy, upcoming surgery, etc.). Some health conditions may make you more susceptible to the side-effects of the drug. Take as directed by your doctor or follow the direction printed on the product insert. Dosage is based on your condition. Tell your doctor if your condition persists or worsens. Important counseling points are listed below.

- Acute hypersensitivity reactions
- Clostridium difficile associated diarrhea
- Consult a doctor in case of second and third trimester of pregnancy
- Consult your doctor if you are on blood thinning drugs such as warfarin
- Development of drug resistant bacteria
- Do not drink alcohol

**CONTRAINDICATION:**

Hypersensitivity to lansoprazole or tinidazole or clarithromycin. Lansoprazole should not be administered with atazanavir. During the first trimester of pregnancy.

**INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:**

If you use other drugs or over the counter products at the same time, the effects of PYLOCIDE KIT may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that you doctor can help you prevent or manage drug interactions. PYLOCIDE KIT may interact with the following drugs and products:

- Acetaminophen
- Alcohol
- Amiodarone
- Amlodipine
- Antacids
- Ascorbic acid

**PREGNACY AND LACTATION:**

Pregnancy

There are no well-controlled studies of lansoprazole or tinidazole or clarithromycin in pregnant women. Clarithromycin is not indicated during pregnancy; hence, this combination is not indicated in pregnancy.

Lactation

There are no well-controlled studies of the use of lansoprazole or tinidazole or clarithromycin during lactation. Tinidazole is excreted in breast milk in concentrations similar to those seen in serum. Since some components of PYLOCIDE KIT are excreted in breast milk, and risk of potential for tumorigenicity shown for lansoprazole in rat carcinogenicity studies, caution should be exercised when administering this kit to a nursing mother.

**ADVERSE REACTION:**

The following is a list of possible side-effects that may occur from all constituting ingredients of PYLOCIDE KIT. This is not a comprehensive list. These side-effects are possible, but do not always occur. Some of the side-effects may be rare but serious. Consult your doctor if you observe any of the following side-effects, especially if they do not go away.

- Furry tongue
- Dark colored urine
- Fever
- Vertigo
- Unpleasant metallic taste
- Nausea

**EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:**

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur. Under these conditions the ability to react may be decreased.

**OVERDOSE:**

- Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of Pylocide Kit, please go to the emergency department of the closest hospital or nursing home. Bring a medicine box, container, or label with you to help doctors with necessary information.
- Do not give your medicines to other people even if you know that they have the same condition or it seems that they may have similar conditions.. This may lead to overdosage.
- Please consult your physician or pharmacist or product package for more information.

**INCOMPATIBILITY:**

Not applicable.

**SHELF LIFE:**

3 Years

**PACKAGING:**

Box of 7 Kits, Alu PVC Blister

**STORAGE CONDITION:**

Store in dry place below 30$^{0}$C.

**DISTRIBUTED BY:**

**Relief Pharma Ltd.**

**MANUFACTURED BY:**

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