1.5.1

Prescribing Information (Summary of Product Characteristics)

1.5.1.1 Name of the medicinal Product

Lansoprazole Delayed Release Capsules USP, Clarithromycin Tablets USP & Tinidazole Tablets (Kit Pack)

1.5.1.2 Qualitative and Quantitative Composition

1.5.1.2.1 Qualitative declaration

Lansoprazole USP +Clarithromycin USP + Tinidazole BP

1.5.1.2.2 Quantitative declaration

For Lansoprazole Delayed-Release Capsules

Sr. No.	Ingredients Chemical Name	Specifications	Quantity (mg/Capsule)	Reason for Inclusion
1.	Lansoprazole Pellets (10.5%w/w)	In-House	286.0	Proton pump Inhibitor
2.	Black/orange Size-"2" hard gelatin empty Capsule	In-House	1.000	Capsule shell
Composition of Lansoprazole Pellets (10.5%w/w)				
3.	Lansoprazole	USP	0.11	Proton pump Inhibitor
4.	Magnesium carbonate	BP	0.017	Diluent
5.	Hypromellose (HPMC E-5)	BP	0.055	Barrier coating agent
6.	Disodium Hydrogen Phosphate	BP	0.006	Buffering agent
7.	Carmellose calcium (Calcium CMC)	BP	0.035	Disintegrating agent
8.	Starch	BP	0.025	Disintegrating agent
9.	Mannitol	BP	0.12	Filler
10.	Sucrose (Pharma grade)	BP	0.332165	Pellets strength enhancer

11.	Sugar spheres (30#40)	BP	0.043	Core pellets
12.	Povidone (K 30)	BP	0.0008	Binder
13.	Sodium Methyl Hydroxybenzoate	BP	0.00003	Preservative
14.	Sodium Propyl Hydroxybenzoate	BP	0.000006	Preservative
15.	Methacrylic acid copolymer L-30D	BP	0.6	Enteric coating agent
16.	Sodium Hydroxide	BP	0.002	pH modifier
17.	Diethyl Phthalate	BP	0.0225	Plasticizer
18.	Purified Talc	BP	0.035	Glidant
19.	Titanium Dioxide	BP	0.015	Coloring agent
20.	Polysorbate 80 (Tween-80)	BP	0.0015	Surfactant

For Clarithromycin Tablets U.S.P. 250 mg

Sr. No.	Ingredients	Specifications	Label Claim (mg/Tablet)	Reason for Inclusion
1.	Clarithromycin	USP	250.0	Macrolide Antibiotic
2.	Colloidal Anhydrous Silica (Aerosil)	BP	5.000	Adsorbent
3.	Partially Pregelatinized Corn Starch (Uni-Pure Dw)	BP	30.00	Binder
4.	Microcrystalline Cellulose (PH 102)	BP	276.0	Diluent
5.	Croscarmellose Sodium	USP-NF	60.00	Disintegrant
6.	Crospovidone (Polyplasdone)	USP-NF	48.00	Disintegrant
7.	Magnesium Stearate	BP	12.00	Lubricant
8.	Purified water	BP	Q.S.	Vehicle
9.	Colour Quinoline yellow SC-SP 2299	In-house	21.000	Binder

10.	Isopropyl Alcohol (IPA)	BP	168.000	Solvent
11.	Dichloromethane (Methylene Dichloride)	BP	252.000	Solvent

For Tinidazole Tablets 500 MG

Sr. No.	Ingredients	Specifications	Label Claim (mg/Tablet)	Reason for Inclusion
1.	Tinidazole	BP	500.000	Anti Parasitic
2.	Lactose (Lactose Monohydrate)	BP	60.000	Diluent
3.	Povidone (P.V.P K-30)	BP	10.000	Binder
4.	Maize starch	BP	30.000	Diluent
5.	Sodium Starch Glycolate (TYPE-A)	BP	12.000	Disintegrant
6.	Purified Talc	BP	6.000	Glidant
7.	Colloidal Anhydrous silica (Aerosil)	BP	7.000	Glidant
8.	Sodium Lauryl sulphate	BP	4.000	surfactant
9.	Microcrystalline Cellulose (PH 101)	BP	66.000	Diluent
10.	Magnesium Stearate	BP	5.000	Lubricant
11.	Colour White SC-SP 3180 (Spraycel)	In-House	20.000	Colouring Agent
12.	Purified Water	BP	Q.S.	Vehicle

1.5.1.3 Pharmaceutical Form

Oral Tablets & Capsule

For Lansoprazole Delayed Release Capsules USP
Black/Orange colour size "2" capsule containing white colour enteric coated pellets.

For Clarithromycin Tablets USP
Yellow coloured, capsule shaped, film coated tablet, plain on both side.

For Tinidazole Tablets

White coloured, capsule shaped, film coated tablets, plain both side.

1.5.1.4 Clinical Particulars

1.5.1.4.1 Therapeutic Indications

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

1.5.1.4.2 Posology and Method of Administration

One LCT 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.

1.5.1.4.3 Contraindications

Hypersensitivity to lansoprazole or tinidazole or clarithromycin.

1.5.1.4.4 Special Warnings and Special Precautions for Use

Lansoprazole: Lansoprazole is hepatically metabolized and studies indicate that it is a weak inducer of Cytochrome P450. There is the possibility of interaction with drugs which are metabolized by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine, theophylline, or warfarin are taken concomitantly with the administration of lansoprazole. No clinically significant effects on NSAIDs or diazepam have been round.

Antacids and sucralfate may reduce the bioavailability of lansoprazole and should, therefore, not be taken within an hour of lansoprazole.

Tinidazole: Drugs of similar chemical structure have been shown to potentiate the effects of oral anticoagulants. Prothrombin times should be closely monitored and adjustments to the dose of the anticoagulant should be made as necessary.

Clarithromycin: Clarithromycin use in patients who are receiving theophylline may be associated with an increase in serum theophylline concentrations.

Concomitant administration or single doses of clarithromycin and carbamazepine has been shown to result in increased plasma concentrations of carbamazepine.

The use of clarithromycin in patients receiving warfarin may result in potentiation of the effects of warfarin. Prothrombin time should be frequently monitored in these patients.

The effects of digoxin may be potentiated with concomitant administration of clarithromycin.

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 preexisting

cardiac abnormalities (arrhythmia, bradycardia, QT interval prolongation, ischemic heart disease, congestive heart failure) or electrolyte disturbances.

The theoretical possibility of ergotism contraindicates the concurrent use of clarithromycin with ergot derivatives.

Clarithromycin increases the serum concentration of cyclosporin hence the dosage of latter may be reduced to avoid renal toxicity.

The use of clarithromycin in patients concurrently taking drugs metabolized by the cytochrome P450 system may be associated with elevations in serum levels of these drugs.

1.5.1.4.5 Interaction with other medicinal products and other forms of interaction

Lansoprazole: Lansoprazole is hepatically metabolized and studies indicate that it is a weak inducer of Cytochrome P450. There is the possibility of interaction with drugs which are metabolized by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine, theophylline, or warfarin are taken concomitantly with the administration of lansoprazole. No clinically significant effects on NSAIDs or diazepam have been round.

Antacids and sucralfate may reduce the bioavailability of lansoprazole and should, therefore, not be taken within an hour of lansoprazole.

Tinidazole: Drugs of similar chemical structure have been shown to potentiate the effects of oral anticoagulants. Prothrombin times should be closely monitored and adjustments to the dose of the anticoagulant should be made as necessary.

Clarithromycin: Clarithromycin use in patients who are receiving theophylline may be associated with an increase in serum theophylline concentrations.

Concomitant administration or single doses of clarithromycin and carbamazepine has been shown to result in increased plasma concentrations of carbamazepine.

The use of clarithromycin in patients receiving warfarin may result in potentiation of the effects of warfarin. Prothrombin time should be frequently monitored in these patients. The effects of digoxin may be potentiated with concomitant administration of clarithromycin. 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 preexisting cardiac abnormalities (arrhythmia, bradycardia, QT interval prolongation, ischemic heart disease, congestive heart failure) or electrolyte disturbances.

The theoretical possibility of ergotism contraindicates the concurrent use of clarithromycin with ergot derivatives.

Clarithromycin increases the serum concentration of cyclosporine hence the dosage of latter may be reduced to avoid renal toxicity. The use of clarithromycin in patients concurrently taking drugs metabolized by the cytochrome P450 system may be associated with elevations in serum levels of these drugs.

1.5.1.4.6 Fertility, 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, 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 LCT Kit in pediatric population has not been established.

Renal And Hepatic impairment: Caution should be exercised while administering LCT Kit with renal impairment and hepatic disease.

1.5.1.4.7 Effects on ability To Drive and use Machines

None.

1.5.1.4.8 Undesirable Effects

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

1.5.1.4.9 Overdose

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

1.5.1.5 Pharmacological Properties

1.5.1.5.1 Pharmacodynamics Properties

Lansoprazole: Lansoprazole is an inhibitor of the gastric H^+,K^+ -ATPase (proton pump). Lansoprazole inhibits gastric acid secretion in a dose related manner irrespective of the source of stimulation. Gastric secretory functions recover gradually following discontinuation of the medicine. Lansoprazole has no effect on histamine, gastrin or cholinergic receptors.

Clarithromycin: Clarithromycin is a semi-synthetic derivative of erythromycin A. It exerts its antibacterial action by binding to the 50s ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis. It is highly potent against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms. The minimum inhibitory concentrations (MICs) of clarithromycin are generally two-told lower than the MICs of erythromycin.

Tinidazole: Tinidazole is a nitroimidazole drug. Tinidazole is bactericidal, amoebicidal and trichomonicidal in action. Tinidazole interferes, inhibits and destroys DNA of cells and causes cellular death.

1.5.1.5.2 Pharmacokinetic Properties

Lansoprazole: It exhibits high (80-90%) bioavailability with a single dose. As a result,

effective acid inhibition is achieved rapidly. Peak plasma levels occurred within 1.5 to 2.0 hours. The plasma elimination half life ranges from I to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. The plasma protein binding is 97%. Following absorption, lansoprazole is extensively metabolized and is excreted by both the renal and biliary route. A study with ^{14}Clabelled lansoprazole indicated that up to 50% of the dose was excreted in the urine. Lansoprazole is metabolized substantially by the liver.

Clarithromycin: Clarithromycin is rapidly and well absorbed from the gastro-intestinal tract after oral administration of Clarithromycin tablets. The microbiologically active metabolite 14-hydroxyclarithromycin is formed by first pass metabolism. Clarithromycin may be given without regard to meals as food does not affect the extent of bioavailability of Clarithromycin tablets. Food does slightly delay the onset of absorption of clarithromycin and formation of the 14-hydroxymetabolite. The pharmacokinetics of clarithromycin are non linear; however, steady-state is attained within 2 days of dosing. At 250 mg b.i.d. 15-20% of unchanged drug is excreted in the urine. With 500 mg b.i.d. daily dosing urinary excretion is greater (approximately 36%). The 14-hydroxyclarithromycin is the major urinary metabolite and accounts for 10-15% of the dose. Most of the remainder of the dose is eliminated in the faeces, primarily via the bile. 5-10% of the parent drug is recovered from tl1e feces.

Clarithromycin is 80% bound to plasma proteins at therapeutic levels.

Tinidazole: It Rapidly and completely absorbed under tasting conditions. Administration with food results in a delay in T "" and a decline in C., .. Plasma protein binding is 12%. It is significantly metabolized in humans prior to excretion. Elimination half-life is 13.2 ± 1.4 hours. Plasma half-life is 12 to 14 hours.

1.5.1.5.3 Preclinical Safety Data

For Lansoprazole Delayed Release Capsules USP

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion.

Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

For Clarithromycin Tablets USP

In acute mouse and rat studies, the median lethal dose was greater than the highest feasible dose for administration (5g/kg).

In repeated dose studies, toxicity was related to dose, duration of treatment and species. Dogs were more sensitive than primates or rats. The major clinical signs at toxic doses included emesis, weakness, reduced food consumption and weight gain, salivation, dehydration and hyperactivity. In all species the liver was the primary target organ at toxic doses. Hepatotoxicity was detectable by early elevations of liver function tests. Discontinuation of the drug generally resulted in a return to or toward normal results. Other tissues less commonly affected included the stomach, thymus and other lymphoid tissues and the kidneys. At near therapeutic doses conjunctival injection and lacrimation occurred only in dogs. At a massive dose of 400mg/kg/day, some dogs and monkeys developed corneal opacities and/or oedema.

Fertility and reproduction studies in rats have shown no adverse effects. Teratogenicity studies in rats (Wistar (p.o.) and Spraque-Dawley (p.o. and i.v.)), New Zealand White rabbits and cynomolgus monkeys failed to demonstrate any teratogenicity from clarithromycin. However, a further similar study in Sprague-Dawley rates indicated a low (6%) incidence of cardiovascular abnormalities which appeared to be due to spontaneous expression of genetic changes. Two mouse studies revealed a variable incidence (3-30%) of cleft palate and embryonic loss was seen in monkeys but only at dose levels which were clearly toxic to the mothers.

For Tinidazole Tablets

Tinidazole has been shown to be mutagenic in some bacterial strains tested in vitro (with and without metabolic activation). Tinidazole was negative for mutagenicity in a

mammalian cell culture system utilising Chinese hamster lung V79 cells (HGPRT test system) and negative for genotoxicity in the Chinese hamster ovary (CHO) sister chromatid exchange assay. Tinidazole was positive for in vivo genotoxicity in the mouse micronucleus assay.

1.5.1.6 Pharmaceutical Particulars

1.5.1.6.1 List of Excipients

For Lansoprazole Delayed Release Capsules USP

Black/orange Size-"2" hard gelatin empty Capsule

For Clarithromycin Tablets USP

Colloidal Anhydrous Silica (Aerosil)
Partially Pregelatinized Corn Starch (Uni-Pure Dw)
Microcrystalline Cellulose(PH 102)
Croscarmellose Sodium
Crospovidone (Polyplasdone)
Magnesium Stearate
Purified water
Colour Quinoline yellow SC-SP 2299
Isopropyl Alcohol (IPA)
Dichloromethane (Methylene Dichloride)

For Tinidazole Tablets

Lactose (Lactose Monohydrate)
Povidone (P.V.P K-30)
Maize starch
Sodium Starch Glycolate
(TYPE-A)
Purified Talc
Colloidal Anhydrous silica (Aerosil)
Sodium Lauryl sulphate

Microcrystalline Cellulose (PH 101)
Magnesium Stearate
Colour White SC-SP 3180 (Spraycel)
Purified Water

1.5.1.6.2 Incompatibilities

Not applicable.

1.5.1.6.3 Shelf Life

24 months

1.5.1.6.4 Special Precautions for Storage

Store under normal storage conditions (15°C- 30°C). Protect from moisture.

1.5.1.6.5 Nature and Contents of Container

1 blister contains 2 Lansoprazole Delayed – Release Capsules USP 30 mg, 2 Clarithromycin Tablets USP 250 mg and 2 Tinidazole Tablets 500 mg. Such 1 blister is packed in a Printed Baby Carton with packaging Insert., Such 7 Baby Carton are packed in a Printed Mother Carton.

1.5.1.6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

1.5.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

1.5.1.7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-02764-665000

Fax: +91-02764-281809
Email: info@lincolnpharma.com
Website: www.lincolnpharma.com

1.5.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-02764-665000
Fax: +91-02764-281809
Email: info@lincolnpharma.com
Website: www.lincolnpharma.com

1.5.1.8 Marketing Authorization Number

To be included after obtaining first registration

1.5.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.5.1.10 Date of Revision of the Text

1.5.1.11 Dosimetry (If Applicable)

Not Applicable

1.5.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable