1.6.1

Prescribing Information (Summary of Product Characteristics)

1.6.1.1 Name of the medicinal Product

Clarithromycin Tablets USP

1.6.1.1.1 Strength

500 mg

1.6.1.1.2 Pharmaceutical Form

Oral Tablet

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Clarithromycin USP

1.6.1.2.2 Quantitative declaration

Sr. No.	Ingredients	Specifications	Label Claim (mg/Tablet)	Reason for Inclusion
1.	Clarithromycin (A)	BP	500.000	Macrolide Antibiotic
2.	Colloidal Anhydrous Silica (Aerosil)	BP	10.000	Adsorbent
3.	Partially Pregelatinized Corn Starch	BP	64.52	Binder
4.	Microcrystalline Cellulose (PH 102)	BP	230.000	Diluent
5.	Croscarmellose Sodium	USP-NF	50.000	Disintegrant
6.	Crospovidone (Polyplasdone)	USP-NF	40.000	Disintegrant
7.	Magnesium Stearate	BP	10.000	Lubricant
8.	Purified water	BP	Q.S.	Vehicle
9.	Colour Quinoline yellow SC-SP 2299	In-house	27.000	Binder
10.	Isopropyl Alcohol (IPA)	BP	216.000	Solvent
11.	Methylene Dichloride	BP	324.00	Solvent

1.6.1.3 Pharmaceutical Form

Oral Tablet

Yellow coloured, capsule shaped, film coated tablet, breakline on one side and plain on other side.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

- Lower respiratory tract infections for example, acute and chronic bronchitis, and pneumonia.
- Upper respiratory tract infections for example, sinusitis and Pharyngitis.
- Skin and soft tissue infections of mild to moderate severity.
- Eradication of H.Pylori in patients with duodenal ulcers

1.6.1.4.2 Posology and Method of Administration

Patients with respiratory infection/skin and soft tissue infection:

Adults: The usual dose is 250 mg twice daily for 7 days although this may be increased to 500 mg twice daily for up to 14 days in severe infections.

Children older than 12 years: As for adults

Children younger than 12 years: Use an appropriate clarithromycin paediatric preparation.

Eradication of H. Pylori in patients with duodenal ulcers (Adults):

Triple Therapy (7-14 days): Clarithromycin 500 mg b.i.d + Lansoprazole 30 mg b.i.d. + Amoxycillin 1000 mg b.i.d.

Triple Therapy (7 days): Clarithromycin 500 mg b.i.d + Lansoprazole 30 mg b.i.d. + Metronidazole 400 mg b.i.d.

Triple Therapy (7 days): Clarithromycin 500 mg b.i.d + Omeprazole 40 mg q.d. + Amoxycillin 1000 mg or Metronidazole 400 mg b.i.d.

Triple Therapy (10 days): Clarithromycin 500 mg b.i.d + Omeprazole 20 mg q.d. + Amoxycillin 1000 mg

Dual Therapy (14 days): Clarithromycin 500 mg t.i.d + Omeprazole 40 mg q.d.

Dosage in renal functional impairment:

Dosage adjustments are not usually required except in patients with severe renal impairment (Creatinine clearance < 30 ml/min). If adjustment is necessary, the total daily dosage should be reduced by half, e.g. 250 mg once daily or 250 mg twice daily in more severe infections.

1.6.1.4.3 Contraindications

- Hypersensitivity to Clarithromycin or other macrolides or any of the Excipients
- In patients with hypokaliemia.

1.6.1.4.4 Special Warnings and Special Precautions for Use

Clarithromycin should not be used in patients with congenital or documented acquired QT prolongation. H. pylori organisms may develop resistance to Clarithromycin. Prolonged or repeated used of Clarithromycin may result in an overgrowth of non-susceptible bacteria or fungi. If super-infection occurs, it should be discontinued and appropriate therapy instituted. Clarithromycin is principally excreted by the liver and kidney. So, caution should be exercised when administered in patients with impaired hepatic or renal function.

Effects on Ability to Drive and Use Machines: None.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

As with other macrolide antibiotics the use of Clarithromycin in patients concurrently taking drugs metabolised by the cytochrome P450 system (e.g. Terfenadin, Astemizol, Alprazolam, Triazolam, Midazolam, Carbamazepine, Phenytoin, Hexobarbital, Pimozide, Disopyramide, Quinidine, Ergot alkaloids, Sildenafil, Lovastatin, Simvastatin, Ciclosporin, Tacrolimus, Methylprednisolone, Alfentanil, Omeprazole, Cisapride, Warfarin, Rifabutin, Vinblastine) may be associated with elevations in serum levels of these drugs. This may result in QT prolongation & cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and Torsade de Points.

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy & lactation: The safety of clarithromycin during pregnancy and breast feeding of infants has not been established. Thus it is not be used during pregnancy or lactation unless the benefit is considered to outweigh the risk. Clarithromycin has been found human milk. So, caution should be exercised when it is administered to nursing women. .

1.6.1.4.7 Effects on ability To Drive and use Machines

None.

1.6.1.4.8 Undesirable Effects

The majority of side effects observed were mild and transient in nature. The most frequently reported events were diarrhea, nausea, abnormal taste, dyspepsia, abdominal pain/discomfort and headache.

1.6.1.4.9 Overdose

Symptoms: gastrointestinal symptoms such as abdominal pain, vomiting, nausea and diarrhea. Treatment: It should be treated by the prompt elimination of unabsorbed drug and supportive measures.

1.6.1.5 Pharmacological Properties

1.6.1.5.1 Pharmacodynamics Properties

Clarithromycin is a semi synthetic derivative of erythromycin-A and is active against wide variety of aerobic and anaerobic gram positive and gram negative bacterial strains. It binds to 50s ribosomal unit of susceptible bacteria and inhibiting protein synthesis. The metabolite 14-hydroxy clarithromycin is also active and synergistic with the parent compound.

1.6.1.5.2 Pharmacokinetic Properties

1.6.1.5.3 Clarithromycin is rapidly and well absorbed from the gastrointestinal tract after oral administration. The microbiologically active metabolite 14-hydroxyclarithromycin is formed by first pass metabolism. KLARO may be given without regard to meals as food does not affect the extent of bioavailability of clarithromycin. Food does slightly delays the onset of absorption of clarithromycin and formation of 14-hydroxymetabolite. The pharmacokinetics of clarithromycin are non linear; steady state is attained within 2 days of dosing. KLARO-250 b.i.d. 15-20% of unchanged drug is excreted in urine. KLARO-500 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 dose. Most of the remainder of the dose is eliminated in the faeces, primarily via the bile.

1.6.1.5.4 Preclinical Safety Data

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

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

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)

1.6.1.6.2 Incompatibilities

Not applicable.

1.6.1.6.3 Shelf Life

36 months

1.6.1.6.4 Special Precautions for Storage

Store under normal storage conditions (l5°C- 30°C). Protect from moisture.

1.6.1.6.5 Nature and Contents of Container

10 Tablets packed in Blister Such a 1 Blister is Packed in Printed Baby Carton With Package Insert.Such a 10 Baby Cartons packed in printed mother carton.

1.6.1.6.6 Special precaution for disposal and other handling

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

1.6.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

1.6.1.7.1 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

1.6.1.7.2 Name and Address of manufacturing site(s)

Lincoln Parenteral Limited
11, 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

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

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

It will be applicable after registration of this product.

1.6.1.10 **Date of Revision of the Text**

1.6.1.11 Dosimetry (If Applicable)

Not Applicable

1.6.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable