1.6.1.1 Name of the medicinal Product

CLARITAB-500 / Clarithromycin Tablets USP 500mg

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	BP	500.0	Active
2.	Microcrystalline cellulose	BP	--	Diluent
3.	Cross Povidone	BP	--	Binder
4.	Tween 80	BP	--	Binder
5.	Iso propyl alcohol	BP	--	Binder
6.	Purified Talc	BP	--	Lubricant
7.	Magnesium Stearate	BP	--	Lubricant
8.	Aerosil	BP	--	Lubricant
9.	Crosscarmellose Sodium	BP	--	Lubricant
10	Titanium dioxide	BP	--	Coating
11	PEG-6000	BP	--	Coating
12	Iso propyl alcohol	BP	--	Solvent
13	Colour : Titatanium Dioxide	IH	--	CoatingMaterial
14	Hydroxy Propyl Methyl Cellulose	BP	--	Film Former

1.6.1.3 Pharmaceutical Form

Oral Tablet

White colored caplet shaped film coated tablet having a break line on one side and other side plain of each tablet.

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

Pharmacotherapeutic group: Antibacterial for systemic use, macrolide
ATC code: J01F A09

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. CLARITAB-500 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. CLARITAB-500 b.i.d. 15-20% of unchanged drug is excreted in urine. CLARITAB-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

Microcrystalline cellulose
Cross Povidone
Tween 80
Iso propyl alcohol
Purified Talc
Magnesium Stearate
Aerosil
Crosscarmellose Sodium
Titanium dioxide

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

Do not Store above 30°C. Protect from moisture.

1.6.1.6.5 Nature and Contents of Container

A blister of 10 Tablets packed , Such 4 blister are packed in carton along with leaflet

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

Merit Organics Ltd
Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,
Dist- Valsad-396155, Gujarat , INDIA

1.6.1.7.2 Name and Address of manufacturing site(s)

Merit Organics Ltd
Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,
Dist- Valsad-396155, Gujarat , INDIA

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