## 1.6 PRODUCT INFORMATION

SPC – Summary of the Product Characteristics

## 1. NAME OF THE MEDICINAL PRODUCT

**ZOLCER KIT**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each kit contains: 2 capsules / 2 tablets each of:

**(A) OMEPRAZOLE DELAYED RELEASE CAPSULES USP 20 mg**

Each capsule contains:

| | |
|---|---|
| Omeprazole USP | 20 mg |
| (enteric coated granules) | |

**(B) TINIDAZOLE TABLETS 500 mg**

Each film-coated tablet contains:

| | |
|---|---|
| Tinidazole BP | 500 mg |
| Excipients | q. s. |

Color: Tartrazine yellow

**(C) CLARITHROMYCIN TABLETS USP 250 mg**

Each film-coated tablet contains:

| | |
|---|---|
| Clarithromycin USP | 250 mg |
| Excipients | q. s. |

Color: Sunset yellow

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Oral tablets and capsules

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**OMEPRAZOLE DELAYED RELEASE CAPSULES USP 20 mg**

It is indicated for the treatment of gastric and duodenal ulcers, arterial or ulcerative reflux, esophagitis, Zollinger- Ellison syndrome. NSAID-induced ulcers.

**TINIDAZOLE TABLETS 500 mg**

**Treatment of the following infections:**

• The eradication of Helicobacter pylori associated with duodenal ulcers, in the presence of antibiotic therapy and acid suppressant therapy.

• Anaerobic infections such as:

Intraperitoneal infections: peritonitis, abscess.

Gynecological infections: endometritis, endomyometritis, ovarian tube abscess.

Bacterial septicemia.
Postoperative wound infections.
Skin and soft tissue infections.
Upper and lower respiratory tract infections: pneumonia, empyema, lung abscess.
• non-specific vaginitis.
• Acute ulcerative gingivitis.
• Urogenital trichomoniasis in men and women.
• Giardiasis.
• Intestinal amebiasis .
• Amoebic involvement of the liver

**Prophylaxis**
Prevention of postoperative infections caused by anaerobic bacteria, in particular those associated with colon, gastrointestinal and gynecological surgery.

**CLARITHROMYCIN TABLETS USP 250 mg**
Clarithromycin tablets are indicated for the treatment of acute and Chronic bacterial infections, when caused by susceptible bacteria.
Lower respiratory tract infections, for example, acute and chronic bronchitis, and pneumonia.
Upper respiratory tract infections, for example, sinusitis and pharyngitis.
Clarithromycin is appropriate for initial therapy in community acquired respiratory infections and has been shown to be active in vitro against common and atypical respiratory pathogens.
Skin and soft tissue infections of mild to moderate severity.
In appropriate combination with antibacterial therapeutic regimens and an appropriate ulcer healing agent for the eradication of H. pylori in patients with H. pylori associated ulcers.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

**4.2 Posology and method of administration**

**OMEPRAZOLE**
Gastric ulcer: 20 mg once daily for 8 weeks. In severe cases, increase to 40 mg once a day.
Reflux gastro - esophageal: 20 mg once per day for 8 weeks. Refractory cases are increasing to 40 mg once daily
Duodenal ulcer: 20 mg once daily for 4 weeks.
Zollinger- Ellison syndrome: 60 mg once daily. maintenance treatment 20-120 mg adjusted for response doses greater than 80 mg per day should be divided into 2 doses.

## TINIDAZOLE

**Dosing instructions**

It is advisable to take tinidazole with food to minimize the incidence of epigastric diseases, discomfort and other gastrointestinal side effects. Food does not affect oral bioavailability of Tinidazole. Alcoholic beverages should be avoided when taking tinidazole and for 3 days afterwards.

**Trichomoniasis**

The recommended dose for women and men is a single oral dose of 2 g to be taken with the food. Since trichomoniasis is a sexually transmitted disease, sexual partners should be treated with the same dose and at the same time.

The recommended dose in adults is a single 2 g dose taken with food. In pediatric patients older than three years of age, the recommended dose is a single dose of 50 mg/kg (up to 2 g) with food.

**Amebiasis**

Intestinal: The recommended dose in adults is a 2 g dose per day for 3 days taken with food. In pediatric patients older than three years of age, the recommended dose is 50 mg/kg/day (up to 2 g per day) for 3 days with food.

Amebic Liver Abscess: The recommended dose in adults is a 2 g dose per day for 3-5 days taken with food. In pediatric patients older than three years of age, the recommended dose is 50 mg/kg/day (up to 2 g per day) for 3-5 days with food. There are limited pediatric data on durations of therapy exceeding 3 days, although a small number of children were treated for 5 days without additional reported adverse reactions. Children should be closely monitored when treatment durations exceed 3 days.

**Bacterial Vaginosis**

The recommended dose in non-pregnant females is a 2 g oral dose once daily for 2 days taken with food or a 1 g oral dose once daily for 5 days taken with food. The use of tinidazole in pregnant patients has not been studied for bacterial vaginosis.

## CLARITHROMYCIN

The dosage of Clarithromycin tablets depends on the clinical condition of the patient and has to be defined in any case by the physician.

Children older than 12 years and adults:

Standard dosage: The usual dose is 250 mg twice daily.

High dosage treatment (severe infections): The usual dose may be increased to 500 mg twice daily in severe infections.

**Elimination of Helicobacter pylori in adults:**

In patients with peptic ulcer due to H. pylori infection, clarithromycin may be used at a dose of 500 mg twice a day during the combination eradication treatment with amoxicillin 1000 mg twice daily and omeprazole 20 mg twice daily.

**Dosage in functional renal failure *:***

The maximum recommended doses should be reduced in proportion to the renal doses. deficiency . The clearance of creatinine is lower than 30 ml / min, the dosage should be in half at 250 mg per day or in the most serious infections at 250 mg twice a day. The duration of treatment should not exceed 14 days in these patients.

**Duration of Treatment:**

The duration of treatment with Clarithromycin tablets depends on the clinical condition of the patient. The duration of treatment must in all cases be determined by the doctor. The usual duration of treatment is 6 to 14 days.

In *pyogenic streptococcus* (like a beta- hemolytic streptococcus) infections, the duration of the treatment must be of at least 10 days.

Combination therapy for the eradication of H. pylori infection, for example clarithromycin 500 mg (two 250 mg tablets or one 500 mg tablet) twice daily in combination with amoxicillin 1000 mg twice daily and omeprazole 20 mg twice daily continued for 7 days .

**4.3 Contraindications**

**OMEPRAZOLE**

Omeprazole is contraindicated in patients with known hypersensitivity to the component of the formulation.

**TINIDAZOLE**

As with other drugs of similar structure, tinidazole is contraindicated in patients having, or with a history of, blood dyscrasia, although no persistent haematological abnormalities have been noted in clinical or animal studies. Tinidazole should be avoided in patients with organic neurological disorders. Tinidazole, other 5-nitroimidazole derivatives or any of the components of this product should not be administered to patients with known hypersensitivity to the drug.

Use of tinidazole is contraindicated during the first trimester of pregnancy and in nursing mothers. See Section 4.6 'Pregnancy and lactation'.

**CLARITHROMYCIN**

•Clarithromycin tablets should not be used in patients with known hypersensitivity to clarithromycin, to other macrolides or to any of the other tablet ingredients.

•Clarithromycin and ergot derivatives should not be co-administered.

•Concomitant administration of clarithromycin and any of the following drugs is contraindicated: cisapride, pimozide and terfenadine. Elevated cisapride, pimozide and terfenadine levels have been reported in patients receiving either of these drugs and clarithromycin concomitantly. This may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and Torsade de Pointes. Similar effects have been observed with concomitant administration of astemizole and other macrolides.

•Clarithromycin should not be administered to hypokalaemic patients (prolongation of QT-time).

**4.4 Special warnings and special precautions for use**

**OMEPRAZOLE**

Amoxicillin - Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. Before initiating therapy with amoxicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids and airway management, including intubation, should also be administered as indicated.
Antimicrobials - Pseudomembranous colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life-threatening.
Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

**TINIDAZOLE**

As with related compounds, alcoholic beverages should be avoided during Tinicrobin therapy because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, tachycardia). Alcohol should be avoided until 72 hours after discontnuing Tinicrobin.
Drugs of similar chemical structure have also produced various neurological disturbances such as dizziness, vertigo, in-coordination and ataxia. If during therapy with Tinicrobin abnormal neurological signs develop, therapy should be discontinued.

**CLARITHROMYCIN**

Due to a potential to increase QT, clarithromycin should be used with care in patients with a history of ventricular arrhythmias, severe cardiac insufficiency, uncorrected hypokalaemia and or hypomagnesaemia, bradycardia (<50 bpm), or during concomitant administration with other medicinal products with a QT-prolonging effect. Clarithromycin should not be used in patients with congenital or documented acquired QT prolongation.
Clarithromycin is principally excreted by the liver and kidney. Caution should be exercised in administering this antibiotic to patients with impaired hepatic or renafunction.
Dosage of Clarithromycin should be suitably reduced depending on the degree of the renal impairment. In elderly patients, the possibility of renal impairment should beconsidered.

H. pylori organisms may develop resistance to clarithromycin.
Patients who are hypersensitive to lincomycin or clindamycin may also be hypersensitive to clarithromycin. Therefore, caution is required when prescribing clarithromycin for such patients.
Prolonged or repeated used of clarithromycin may result in an overgrowth of non - susceptible bacteria or fungi. If super-infection occurs, clarithromycin should be discontinued and appropriate therapy instituted.
Pseudomembranous colitis has been reported with the use of broad-spectrum antibiotics. Therefore, it is important to consider its diagnosis in patients who develop severe diarrhoea during or after therapy with clarithromycin.

**4.5 Interaction with other medicinal products and other forms of Interaction**
**Omeprazole**
Omeprazole may reduce the absorption of ketoconazole, itraconazole, posaconazole, erlotinib when used concomitantly. Co-administration of Omeprazole with atazanavir is not recommended. Concurrent administration with MAO inhibitors is not recommended.
**Tinidazole**
Alcohol: Concurrent use of tinidazole and alcohol may produce a disulfiram-like reaction and should be avoided. Anticoagulants: 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**
The use of the following drugs is strictly contraindicated due to the potential for severe drug interaction effects: Cisapride, pimozide, astemizole and terfenadine, Ergotamine/dihydroergotamine, Effects of Other Medicinal Products on Clarithromycin. Efavirenz, nevirapine, rifampicin, rifabutin and rifapentine, Fluconazole.

**4.6 Pregnancy and lactation**

**Pregnancy**
**Teratogenic effects**
**Pregnancy category C:**
Four teratogenicity studies in rats (three with oral doses and one with intravenous doses up to 160 mg/kg/day administered during the period of major organogenesis) and two in rabbits at oral doses up to 125 mg/kg/day (approximately 2 times the recommended maximum human dose based on mg/m2) or intravenous doses of 30 mg/kg/day administered during gestation days 6 to 18 failed to demonstrate any teratogenicity from clarithromycin. Two additional oral studies in a different rat strain at similar doses and similar conditions demonstrated a low incidence of cardiovascular anomalies at doses of 150 mg/kg/day administered during gestation days 6 to 15. Plasma levels after 150 mg/kg/day were 2 times the human serum levels.
Four studies in mice revealed a variable incidence of cleft palate following oral doses

of 1000 mg/kg/day (2 and 4 times the recommended maximum human dose based on mg/m2, respectively) during gestation days 6 to 15. Cleft palate was also seen at 500 mg/kg/day. The 1000 mg/kg/day exposure resulted in plasma levels 17 times the human serum levels. In monkeys, an oral dose of 70 mg/kg/day (an approximate equidose of the recommended maximum human dose based on mg/m2) produced fetal growth retardation at plasma levels that were 2 times the human serum levels.
There are no adequate and well-controlled studies in pregnant women. Clarithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing mothers**
It is not known whether clarithromycin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when clarithromycin is administered to a nursing woman. It is known that clarithromycin is excreted in the milk of lactating animals and that other drugs of this class are excreted in human milk. Preweaned rats, exposed indirectly via consumption of milk from dams treated with 150 mg/kg/day for 3 weeks, were not adversely affected, despite data indicating higher drug levels in milk than in plasma.

**Pediatric Use**
Safety and effectiveness of clarithromycin in pediatric patients under 6 months of age have not been established. The safety of clarithromycin has not been studied in MAC patients under the age of 20 months. Neonatal and juvenile animals tolerated clarithromycin in a manner similar to adult animals. Young animals were slightly more intolerant to acute overdosage and to subtle reductions in erythrocytes, platelets and leukocytes but were less sensitive to toxicity in the liver, kidney, thymus, and genitalia.

**4.7 Effects on ability to drive and use machines**
None

**4.8 Undesirable effects**
**Omeprazole:**
diarrhoea, dizziness, pruritus, skin rashes, GIT infections; anaphylaxis, angioedema, chest pain, dyspnoea, erythema multiforme, gastroenteritis, hyperglycaemia, infection, injection site reaction, jaundice, optic neuropathy, anterior ischaemia, pancreatitis, speech disorder.
**Tinidazole:**
side effects have generally been infrequent, mild and self-limiting. Blood and lymphatic system disorders, Nervous System, Gastrointestinal disorders, Skin and subcutaneous tissue disorders: hypersensitivity reactions, occasionally severe, may occur in rare cases in the form of skin rash, pruritus, urticaria and angioneurotic edema. Renal and Urinary disorders: dark urine. General disorders and administration site conditions: fever, tiredness.

**Clarithromycin:**
The most frequent and common adverse reactions related to clarithromycin therapy for both adult and peadiatric populations are abdominal pain, diarrhoea, nausea, vomiting

and taste perversion. These adverse reactions are usually mild in intensity and are consistent with the known safety profile of macrolide antibiotics. There was no significant difference in the incidence of these gastrointestinal adverse reactions during clinical trials between the patient population with or without pre-existing mycobacterial infections.

**4.9 Overdose**

In the event of over dosage of Omeprazole gastric lavage should be performed. Signs and symptoms of over dosage there are no reported overdoses in humans with Tinidazole. Clarithromycin to produce gastro-intestinal symptoms. One patient who had a history of bipolar disorder ingested 8 grams of clarithromycin and showed altered mental status, paranoid behavior, hypokalemia and hypoxemia.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:**
Therapeutic Class: **Omeprazole** is a proton pump inhibitor
Omeprazole Delayed-Release Capsules USP 20 mg used for Gastric ulcer.
**ATC CODE**: A02BC01
Therapeutic Class: **Tinidazole** is an anti-parasitic drug
Tinidazole Tablets 500 mg used for parasitic infection.
**ATC CODE**: DB00911

Therapeutic Class: **Clarithromycin** is a macrolide antibiotic
Clarithromycin Tablets USP 250 mg used for acute and chronic bacterial infections
**ATC CODE:** DB01211

**OMEPRAZOLE**
Omeprazole 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 gastric mucosa, omeprazole 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 acid secretion irrespective of the stimulus. Animal studies indicate that after rapid disappearance from plasma, omeprazole can be found within the gastric mucosa for a day or more.

**TINIDAZOLE**
Tinicrobin is active against both protozoa and obligate anaerobic bacteria. The activity against protozoa involves Trichomonas vaginalis, Entamoeba histolytica and Giardia lamblia.
The mode of action of Tinicrobin against anaerobic bacteria and protozoa involves penetration of the drug into the cell of the micro-organism and subsequent damage of DNA strands or inhibition of their synthesis.
Tinicrobin is active against Helicobacter pylori, Gardnerella vaginalis and most anaerobic bacteria including Bacteroides fragilis, Bacteroides melaninogenicus, Bacteroides spp., Clostridium spp., Eubacterium spp., Fusobacterium spp., Peptococcus spp., Peptostreptococcus spp. and Veillonella spp. Helicobacter pylori (H. pylori) is associated with acid peptic disease including duodenal ulcer and gastric ulcer in which about 95% and 8 % of patients respectively are infected with this agent. H. pylori is also implicated as a major contributing factor in the development of gastritis and ulcer recurrence in such patients. Evidence suggests a causative link between H. pylori and gastric carcinoma.
Clinical evidence has shown that the combination of Tinicrobin with omeprazole and

clarithromycin eradicates 91-96% of H. pylori isolates. Various different H. pylori eradication regimens have shown that eradication of H. pylori heals duodenal ulcers and reduces the risk of ulcer recurrence.

**CLARITHROMYCIN**

Clarithromycin prevents bacteria from growing by interfering with their protein synthesis. Clarithromycin binds to the subunit 50S of the bacterial ribosome and thus inhibits the translation of peptides. Clarithromycin has similar antimicrobial spectrum as erythromycin but is more effective against certain gram-negative bacteria, particularly Legionella pneumophila. Besides this bacteriostatic effect, clarithromycin also has bactericidal effect on certain strains such as Haemophilus influenzae, Streptococcus pneumoniae and Neisseria gonorrhoeae.

**5.2 Pharmacokinetic properties**

**OMEPRAZOLE**

**Absorption**

Omeprazole Delayed-Release Capsules contain an enteric-coated microtablet formulation of omeprazole (because omeprazole is acid-labile), so that absorption of omeprazole begins only after the microtablets leave the stomach. Absorption is rapid, with peak plasma levels of omeprazole occurring within 0.5 to 3.5 hours. Peak plasma concentrations of omeprazole and AUC are approximately proportional to doses up to 40 mg, but because of a saturable first-pass effect, a greater than linear response in peak plasma concentration and AUC occurs with doses greater than 40 mg. Absolute bioavailability (compared with intravenous administration) is about 30-40% at doses of 20-40 mg, due in large part to presystemic metabolism. In healthy subjects the plasma half-life is 0.5 to 1 hour, and the total body clearance is 500-600 mL/min.

The bioavailability of omeprazole increases slightly upon repeated administration of Omeprazole Delayed-Release Capsules.

Omeprazole Delayed-Release Capsules 40 mg was bioequivalent when administered with and without applesauce. However, Omeprazole Delayed-Release Capsules 20 mg was not bioequivalent when administered with and without applesauce. When administered with applesauce, a mean 25% reduction in Cmax was observed without a significant change in AUC for Omeprazole Delayed-Release Capsules 20 mg. The clinical relevance of this finding is unknown.

**Distribution**

Protein binding is approximately 95%.

**Metabolism**

Omeprazole is extensively metabolized by the enzyme cytochrome P450 (CYP) enzyme system.

**Excretion**

Following single dose oral administration of a buffered solution of omeprazole, little if any unchanged drug was excreted in urine. The majority of the dose (about 77%) was eliminated in urine as at least six metabolites. Two were identified as hydroxyomeprazole and the corresponding carboxylic acid. The remainder of the dose was recoverable in feces. This implies a significant biliary excretion of the metabolites of omeprazole. Three metabolites have been identified in plasma — the sulfide and sulfone derivatives of omeprazole, and hydroxyomeprazole. These metabolites have very little or no antisecretory activity.

**TINIDAZOLE**

**Absorption:**

After oral administration, tinidazole is rapidly and completely absorbed.

A bioavailability study of Tindamax (tinidazole) tablets was conducted in adult healthy volunteers. All subjects received a single oral dose of 2 g (four 500 mg tablets) of Tindamax (tinidazole) following an overnight fast. Oral administration of four 500 mg tablets of Tindamax (tinidazole) under fasted conditions produced a mean peak plasma concentration (Cmax) of 47.7 (±7.5) µg/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 (AUC, 0-∞) of 901.6 (± 126.5) µg/hr/mL at 72 hours. The elimination half-life (T½) was 13.2 (±1.4) hours. Mean plasma levels decreased to 14.3 µg/mL at 24 hours, 3.8 µg/mL at 48 hours and 0.8 µg/mL at 72 hours following administration. Steady-state conditions are reached in 2½ - 3 days of multi-day dosing.

Administration of Tindamax (tinidazole) tablets with food resulted in a delay in Tmax of approximately 2 hours and a decline in Cmax of approximately 10%, compared to fasted conditions. However, administration of Tindamax (tinidazole) with food did not affect AUC or T½ in this study.

In healthy volunteers, administration of crushed Tindamax (tinidazole) tablets in artificial cherry syrup, [prepared as described in after an overnight fast had no effect on any pharmacokinetic parameter as compared to 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 CYP3A4. In an in vitro metabolic drug interaction study, tinidazole concentrations of up to 75 µg/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 12-14 hours. Tinidazole is excreted by the liver and the kidneys. Tinidazole is excreted in the urinemainly as unchanged drug (approximately 20-25% of the administered dose).Approximately 12% of the drug is excreted in the feces.

**CLARITHROMYCIN**
**Absorption:**
Clarithromycin is rapidly and well absorbed from the gastrointestinal tract – primarily in the jejunum - after oral administration. Due to its chemical structure (6-O-Methylerythromycin) clarithromycin is quite resistant to degradation by stomach acid. Serum levels of 1 – 2 µg/ml clarithromycin were observed in adults after oral administration of 250 mg twice daily. After administration of 500 mg clarithromycin twice daily serum levels of 2,8 µg/ml were obtained.
After administration of 250 mg clarithromycin twice daily the pharmacological active 14-hydroxy metabolite attains peak plasma concentrations of 0,6 µg/ml.

**Distribution:**
Clarithromycin gives good penetration into different compartments. Therapeutic drug levels exceeding the minimum inhibitory levels for common pathogens can be rapidly achieved. Clarithromycin provides tissue concentrations that are several times higher than the circulating drug levels. Increased levels have been found in both tonsillar and lung tissue. Clarithromycin also penetrates the gastric mucus.
Clarithromycin is 80% bound to plasma proteins at therapeutic levels.

**Half- Life Serum:**
The serum half-life of the active 14-(R)-hydroxy metabolite ranges between 5 to 6 hours.

**Biotransformation And Elimination:**
Clarithromycin is rapidly and extensively metabolised in the liver. Metabolism involves mainly N-dealkylation, oxidation and stereospecific hydroxylation at position C 14.

After oral administration of radioactive clarithromycin 70 - 80% of the radioactivity was found in the faeces. Approximately 20 -30% of clarithromycin is collected as the unchanged parent molecule in the urine. This proportion is increased when the dose is increased. Renal insufficiency increases clarithromycin levels in plasma, if the dose is not decreased.

The pharmacokinetics of clarithromycin are non-linear. This is an indication for a saturation of hepatic metabolism at high doses; however, steady state is attained within 2 days of dosing.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients

| Sr. No. | Raw materials | Pharmacopoeia |
|---|---|---|
| 1. | Non Pareil Seed 12#/16#** | IHS |
| 2. | Hard Gelatin Capsule Shells Size "2" Dark Blue/ Light Blue | IHS |
| 3. | Maize Starch* | BP |
| 4. | Purified Water** | BP |
| 5. | Methyl Hydroxybenzoate | BP |
| 6. | Propyl Hydroxybenzoate | BP |
| 7. | Gelatin | BP |
| 8. | Purified Talc | BP |
| 9. | Magnesium Stearate | BP |
| 10. | Sodium Starch Glycolate (Type A) | BP |
| 11. | Colloidal Anhydrous Silica | BP |
| 12. | Hypromellose*** | BP |
| 13. | Isopropyl Alcohol ** | BP |
| 14. | Dichloromethane** | BP |
| 15. | Diethyl Phthalate *** | BP |
| 16. | Titanium Dioxide*** (Colour code index: 77891) | BP |
| 17. | Colour Tartrazine Yellow Lake *** (Colour Code Index: 19140) | IHS |
| 18. | Microcrystalline Cellulose * | BP |
| 19. | Pregelatinised Starch | BP |
| 20. | Croscarmellose Sodium | BP |
| 21. | Calcium Stearate | BP |
| 22. | Instacoat Universal | IHS |

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

24 months

### 6.4 Special precautions for storage

Store below 30°C. Protect from moisture.

### 6.5 Nature and contents of container

Each kit contains: 2 capsules of omeprazole /2 tablets each of Tinidazole & Clarithromycin in Blister & 7 such kit in a Carton.

### 6.6 Instructions for use and handling

No special requirements

### 7. Marketing Authorization Holder

**AUROCHEM LABORATORIES (INDIA) PVT. LTD.**
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website: www.aurochemlaboratories.com

### 8. Marketing Authorization Number (S)

Form 28A in KD/887-A

### 9. Date of First Authorization/Renewal of the Authorization

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### 10. Date of Revision of the Text

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