

## TRIOPAC

## Triple Therapy

### Composition

Amoxitid 500 mf capsules: Each capsule contains 500 mg Amoxicillin.

Laricid 500 mg tablets: Each tablet contains 500 mg Clarithromycin.

Mepral 20 mg capsules: Each capsule contains 20 mg Omeprazole.

### Action

#### Amoxitid 500 mg capsules

Amoxicillin is similar to ampicillin in its bactericidal action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide.

Amoxicillin has been shown to be active against *Helicobacter pylori*

Microorganisms

#### Laricid 500 mg tablets

Clarithromycin exerts its antibacterial action by binding to the 50S ribosomal subunit of susceptible microorganisms resulting in inhibition of protein synthesis. Clarithromycin has been shown to be active against *Helicobacter pylori* microorganisms.

#### Mepral 20 mg capsules

Omeprazole belongs to a new class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H<sub>2</sub> histamine antagonistic properties, but that suppress gastric acid secretion by specific inhibition of the H<sup>+</sup>/K<sup>+</sup> 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.

### Indications

Treatment of patients with *H. pylori* infection and duodenal ulcer disease (active or 1 year history of a duodenal ulcer) to eradicate *H. pylori*. Eradication of *H. pylori* has been shown to reduce the risk of duodenal ulcer recurrence.

### Contraindications

Triopac administration with cisapride, pimozide, astemizole, or terfenadine is contraindicated. There have been post-marketing reports of drug interactions when clarithromycin and/or erythromycin are co-administered with cisapride, pimozide, astemizole, or terfenadine resulting in cardiac arrhythmias (QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsades de pointes) most likely due to inhibition of metabolism of these drugs by erythromycin and clarithromycin. Fatalities have been reported.

### Warnings and Precautions

#### Triopac (as for Clarithromycin)

Prescribing (Triopac) in the absence of a proven or strongly suspected bacterial infection or a prophylactic indications is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

**CLARITHROMYCIN SHOULD NOT BE USED IN PREGNANT WOMEN EXCEPT IN CLINICAL CIRCUMSTANCES WHERE NO ALTERNATIVE THERAPY IS APPROPRIATE. IF PREGNANCY OCCURS WHILE TAKING THIS DRUG, THE PATIENT SHOULD BE APPRISED OF THE POTENTIAL HAZARD TO THE FETUS.**

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin, 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.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

### **General**

Clarithromycin is principally excreted via the liver and kidney. Clarithromycin may be administered without dosage adjustment to patients with hepatic impairment and normal renal function. However, in the presence of severe renal impairment with or without coexisting hepatic impairment, decreased dosage or prolonged dosing intervals may be appropriate.

Clarithromycin in combination with ranitidine and bismuth citrate therapy is not recommended in patients with creatinine clearance less than 25 ml/min.

Clarithromycin in combination with ranitidine bismuth citrate should not be used in patients with a history of acute porphyria.

For information about precautions of other drugs indicated in combination with clarithromycin serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, I.V. steroids, and airway management, including intubation, should also be administered as indicated.

### **Pregnancy**

#### *Category C*

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 unknown 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.

### **Geriatric Use**

In clinical trials, elderly patients did not have an increased incidence of adverse events when compared to younger patients. Dosage adjustment should be considered in elderly patients with severe renal impairment.

### **Adverse Reactions**

The most frequent adverse reactions for the triple therapy are diarrhea, taste perversion, and headache.

### **Drug Interactions**

#### **Amoxicillin**

Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use of amoxicillin and probenecid may result in increased and prolonged blood levels of amoxicillin.

Chloramphenicol, macrolides, sulfonamides, and tetracyclines may interfere with the bactericidal effects of penicillin. This has been demonstrated *in vitro*; however, the clinical significance of this interaction is not well documented.

#### **Clarithromycin**

*Astemizole, cisapride, pimozide and terfenadine*

Has resulted in cardiac arrhythmias, including QTc-interval prolongation, ventricular arrhythmia, ventricular tachycardia, ventricular fibrillation, and torsade de pointes. Fatalities have occurred. The most likely cause is the inhibition of metabolism of these medicines by Clarithromycin. Concurrent use is contra-indicated.

#### *Anticoagulants such as warfarin*

Clarithromycin may result in the potentiation of the effects of warfarin. Prothrombin time should be monitored closely.

#### *Digoxin*

Clarithromycin has been shown to increase serum digoxin concentrations. Monitoring of digoxin serum concentrations is recommended.

*Carbamazepine or other medicines metabolized by the cytochrome P450 enzyme system for example, alprazolam, cyclosporine, disopyramide, ergot alkaloids, methylprednisolone, midazolam, omeprazole, quinidine, sildenafil, simvastatin, tacrolimus, triazolam, vinblastine, phenytoin, and valproate*

Clarithromycin may be associated with increased levels of these medicines. Serum concentrations of these medicines may require monitoring. Rhabdomyolysis has been reported with concomitant use of Clarithromycin and the HMGCoA reductase inhibitors e.g. simvastatin.

#### *Rifabutin and Rifampicin*

May decrease serum concentration of Clarithromycin by >50%. Co-administration has been reported to cause a higher incidence of uveitis compared to rifabutin alone.

### **Omeprazole**

#### *Omeprazole/ Diazepam/ Phenytoin*

Omeprazole can prolong the elimination of drugs that are metabolized by oxidation in the liver, e.g. diazepam and phenytoin. It is recommended to monitor patients receiving phenytoin concomitantly with omeprazole. A reduction of the phenytoin dose may be necessary.

#### *Omeprazole/ Theophylline/ Warfarin*

No interaction with theophylline has been found, but there may be interactions with other drugs also metabolized via the cytochrome P-450 enzyme system, such as warfarin.

#### *Omeprazole/ Antacids*

No interaction with concomitantly administered antacids has been found.

#### *Omeprazole/ Drugs whose Absorption is pH-Dependent*

By increasing gastric pH, omeprazole has the potential to affect the bioavailability of any medication whose absorption is pH-dependent (e.g. Ketoconazole, Ampicillin esters and iron salts).

## **Dosage and Administration**

### **H. pylori Eradication for the Reduction of the Risk of Duodenal Ulcer Recurrence**

#### **Triopac (Omeprazole/Clarithromycin/Amoxicillin)**

The recommended adult oral regimen is Omeprazole 20 mg plus Clarithromycin 500 mg plus Amoxicillin 1000 mg each given twice daily for 7-14 days.

## **Presentation**

Each carton contains 7 internal unit packs sachets, each contains 4 capsule of Amoxitid 500 mg, 2 capsules of Mepreal 20 mg and 2 tablets of Laricid 500 mg.