

## PACKAGE LEAFLET – INFORMATION FOR THE USER

### **Maclar 500** **Clarithromycin Tablets USP 500 mg**

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to you doctor or pharmacist. This includes any possible side effects not listed in the leaflet.

#### **What is in this leaflet:**

1. What Clarithromycin Tablets are and what they are used for
2. What you need to know before you take Clarithromycin Tablets
3. How to take Clarithromycin Tablets
4. Possible side effects
5. How to store Clarithromycin Tablets
6. Contents of the pack and other Information.

#### **1. What Clarithromycin Tablets are and what they are used for**

Clarithromycin belongs to a group of medicine called macrolide antibiotics. Antibiotics stop the growth of bacteria which cause infections.

Clarithromycin is used to treat following mild to moderate infections caused by designated, susceptible bacteria:

- Acute Bacterial Exacerbation of Chronic Bronchitis in Adults
- Acute Maxillary Sinusitis
- Community-Acquired Pneumonia
- Pharyngitis/Tonsillitis
- Uncomplicated Skin and Skin Structure Infections
- Acute Otitis Media in Pediatric Patients
- Treatment and Prophylaxis of Disseminated Mycobacterial Infections
- *Helicobacter pylori* Infection and Duodenal Ulcer Disease in Adults

#### **2. What you need to know before you take clarithromycin**

##### **Do not take Clarithromycin Tablets if you:**

- Are hypersensitive to clarithromycin, erythromycin or any of the macrolide antibacterial drugs.
- Are pregnant women Are receiving drugs with known prolongation of the QT interval, ventricular cardiac arrhythmia, including torsades de pointes
- Are receiving drugs known to prolong the QT interval

- have ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia and in patients receiving Class IA (e.g., quinidine, procainamide, disopyramide) or Class III (e.g., dofetilide, amiodarone, sotalol) antiarrhythmic agents.
- Use of clarithromycin with lomitapide, simvastatin, lovastatin, ergotamine, dihydroergotamine, cisapride, pimozide is contraindicated. Co-administration of clarithromycin with cisapride or pimozide, resulting in cardiac arrhythmias (QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsades de pointes).
- Are taking medicines called lomitapide, lovastatin, and simvastatin.
- Are taking medicines called ergot alkaloids (ergotamine/dihydroergotamine).
- Have abnormally low levels of potassium or magnesium in the blood (a condition is known as hypokalaemia or hypomagnesemia).
- Are taking colchicine in renal or hepatic impairment.
- Have history of cholestatic jaundice/hepatic dysfunction associated with prior use of clarithromycin.
- Are concomitantly receiving clarithromycin and ergotamine or dihydroergotamine or combination with other drugs may contraindicated

### **Warnings and precautions:**

Talk to your doctor or pharmacist before taking Clarithromycin tablets:

- If you are suffering from the event of severe acute hypersensitivity reactions, such as anaphylaxis, Stevens-Johnson Syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), Henoch-Schonlein purpura, and acute generalized exanthematous pustulosis, discontinue clarithromycin therapy immediately and institute appropriate treatment
- If you have low levels of magnesium or potassium.
- If you are suffering from bradycardia (slow heart rate) or irregular heartbeat
- If you have any hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice
- Suffering from symptoms of hepatitis can include anorexia, jaundice, dark urine, pruritus, or tender abdomen. Discontinue clarithromycin immediately if signs and symptoms of hepatitis occur.
- Suffering from Myasthenia Gravis (weakness of the skeletal (voluntary) muscles).
- Suffering from *Clostridium difficile* associated diarrhea (CDAD).
- If you have suspected or confirmed coronary artery disease to continue medications and lifestyle modifications for their coronary artery disease because clarithromycin may be associated with increased risk for mortality years after the end of clarithromycin treatment.
- If you are taking concomitantly with CYP3A4 substrates e.g. colchicine, lomitapide, simvastatin, lovastatin, atorvastatin, disopyramide, calcium channel blockers metabolized by CYP3A4 (e.g., verapamil, amlodipine, diltiazem, nifedipine), oral hypoglycemic agents e.g. nateglinide, pioglitazone, repaglinide and rosiglitazone, and/or insulin, quetiapine, oral anticoagulants e.g. warfarin, benzodiazepines (e.g. triazolobenzodiazepines, such as triazolam and midazolam)

- You have risk of the development of drug-resistant bacteria
- *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.

**Other medicines and Clarithromycin tablets:**

Tell your doctor if you are taking, have recently taken or might take any of the following medicines as your dose may need to be changed or you may need to have regular tests performed.

- Antiarrhythmics: Disopyramide, Quinidine, Dofetilide, Amiodarone, Sotalol, Procainamide, Digoxin
- Oral Anticoagulants: Warfarin
- Antiepileptics: Carbamazepine
- Antifungals: Itraconazole, Fluconazole
- Anti-Gout Agents: Colchicine (in patients with renal or hepatic impairment), Colchicine (in patients with normal renal and hepatic function)
- Antipsychotics: Pimozide, Quetiapine
- Antispasmodics: Tolterodine (patients deficient in CYP2D6 activity)
- Antivirals: Atazanavir, Saquinavir (in patients with decreased renal function), Ritonavir, Etravirine, Maraviroc, Boceprevir, Didanosine, Zidovudine
- Calcium Channel Blockers: Verapamil, Amlodipine, Diltiazem, Nifedipine
- Ergot Alkaloids: Ergotamine, Dihydroergotamine
- Gastroprokinetic Agents: Cisapride
- Lipid-lowering agents: Lomitapide, Lovastatin, Simvastatin, Atorvastatin, Pravastatin, Fluvastatin
- Hypoglycemic Agents: Nateglinide, Pioglitazone, Repaglinide, Rosiglitazone, Insulin
- Immunosuppressants: Cyclosporine, Tacrolimus
- Phosphodiesterase inhibitors: Sildenafil, Tadalafil, Vardenafil
- Proton Pump Inhibitors: Omeprazole
- Xanthine Derivatives: Theophylline
- Triazolobenzodiazepines and Other Related Benzodiazepines: Midazolam, Alprazolam, Triazolam, Temazepam, Nitrazepam, Lorazepam
- Cytochrome P450 Inducers: Rifabutin
- Other Drugs Metabolized by CYP3A: Alfentanil, Bromocriptine, Cilostazol, Methylprednisolone, Vinblastine, Phenobarbital, St. John's Wort
- Other Drugs Metabolized by CYP450 Isoforms Other than CYP3A: Hexobarbital, Phenytoin, Valproate
- Antifungals: Itraconazole
- Antivirals: Atazanavir, Ritonavir (in patients with decreased renal function), Saquinavir (in patients with decreased renal function), Etravirine, Saquinavir (in patients with normal renal function), Ritonavir (in patients with normal renal function)
- Proton Pump Inhibitors: Omeprazole

- Miscellaneous Cytochrome P450 Inducers: Efavirenz, Nevirapine, Rifampicin, Rifabutin, Rifapentine

You should not take Clarithromycin tablets if you are taking any of the medicines listed in the section above.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including those obtained without a prescription.

### **Taking Clarithromycin Tablets with food**

Clarithromycin Tablets may be taken with or without food.

### **Pregnancy, breast-feeding and fertility**

Clarithromycin is not recommended for use in pregnant women except in clinical circumstances where no alternative therapy is appropriate. No data are available to assess the effects of clarithromycin on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for clarithromycin and any potential adverse effects on the breast-fed child from clarithromycin or from the underlying maternal condition.

Ask your doctor or pharmacist for advice before taking any medicine

### **Driving and using machines**

There are no data on the effect of clarithromycin on the ability to drive or use machines. However, the potential for dizziness, vertigo, confusion and disorientation, which may occur with the clarithromycin. The potential for these adverse reactions should be taken into account before patients drive or use machines.

## **3. How to take Clarithromycin Tablets**

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The dose of Clarithromycin varies with the condition being treated. The dose you should take will be on the pharmacist's label. Always take the tablets exactly as your doctor has told you to. You should check with your doctor or pharmacist if you are not sure.

### Important Administration Instructions

Clarithromycin tablet 500mg can be taken with or without food and can be taken with milk.

### Adult Dosage

The recommended dosages of Clarithromycin Tablets for the treatment of mild to moderate infections in adults are listed in Table below.

### Adult Dosage Guidelines for Clarithromycin Tablets

Infection	Dosage (every 12 hours)	Duration (days)
Acute bacterial exacerbation of chronic bronchitis	250 to 500 mg <sup>a</sup>	7 <sup>b</sup> -14
Acute maxillary sinusitis	500 mg	14
Community-acquired pneumonia	250 mg <sup>c</sup>	7 <sup>d</sup> -14
Pharyngitis/Tonsillitis	250 mg	10
Uncomplicated skin and skin structure infections	250 mg	7-14
Treatment and prophylaxis of disseminated <i>Mycobacterium avium</i> disease	500 mg <sup>e</sup>	-
<i>H.pylori</i> eradication to reduce the risk of duodenal ulcer recurrence with amoxicillin and omeprazole or lansoprazole	500 mg	10-14
<i>H.pylori</i> eradication to reduce the risk of duodenal ulcer recurrence with omeprazole	500 mg every 8 hours	14

a For *M. catarrhalis* and *S. pneumoniae* use 250 mg. For *H. influenzae* and *H. parainfluenzae*, use 500 mg.  
b For *H. parainfluenzae*, the duration of therapy is 7 days.  
c For *H. parainfluenzae* and *M. catarrhalis* use clarithromycin ER tablets only.  
d For *H. influenzae*, the duration of therapy is 7 days.  
e Clarithromycin therapy should continue if clinical response is observed. Clarithromycin can be discontinued when the patient is considered at low risk of disseminated infection.

#### Combination Dosing Regimens for *H. pylori* Infection

- **Triple therapy: Clarithromycin tablets /lansoprazole/amoxicillin**  
The recommended adult dosage is 500 mg Clarithromycin tablets, 30 mg lansoprazole, and 1 gram amoxicillin, all given every 12 hours for 10 or 14 days.
- **Triple therapy: Clarithromycin tablets /omeprazole/amoxicillin**  
The recommended adult dosage is 500 mg Clarithromycin tablets, 20 mg omeprazole, and 1 gram amoxicillin; all given every 12 hours for 10 days. In patients with an ulcer present at the time of initiation of therapy, an additional 18 days of omeprazole 20 mg once daily is recommended for ulcer healing and symptom relief.
- **Dual therapy: Clarithromycin tablets /omeprazole**  
The recommended adult dosage is 500 mg Clarithromycin tablets given every 8 hours and 40 mg omeprazole given once every morning for 14 days. An additional 14 days of omeprazole 20 mg once daily is recommended for ulcer healing and symptom relief.

#### Pediatric Dosage

The recommended daily dosage is 15 mg/kg/day divided every 12 hours for 10 days (up to the adult dose). Refer to dosage regimens for mycobacterial infections in pediatric patients for additional dosage information.

#### Dosage Regimens for Mycobacterial Infections

For the treatment of disseminated infection due to MAC, Clarithromycin tablets are recommended as the primary agents. Clarithromycin tablets should be used in combination with other antimycobacterial drugs (e.g. ethambutol) that have shown *in vitro* activity against MAC or clinical benefit in MAC treatment.

### Adult Patients

For treatment and prophylaxis of mycobacterial infections in adults, the recommended dose of Clarithromycin is 500 mg every 12 hours.

### Pediatric Patients

For treatment and prophylaxis of mycobacterial infections in pediatric patients, the recommended dose is 7.5 mg/kg every 12 hours up to 500 mg every 12 hours.

Clarithromycin therapy should continue if clinical response is observed. Clarithromycin can be discontinued when the patient is considered at low risk of disseminated infection.

### Dosage Adjustment in Patients with Renal Impairment

See Table below for dosage adjustment in patients with moderate or severe renal impairment with or without concomitant atazanavir or ritonavir-containing regimens.

#### **Clarithromycin Dosage Adjustments in Patients with Renal Impairment**

Patients with severe renal impairment (CL <sub>cr</sub> of <30 mL/min)	Reduce the dosage of Clarithromycin by 50%
Patients with moderate renal impairment (CL <sub>cr</sub> of 30 to 60 mL/min) taking concomitant atazanavir or ritonavir-containing regimens	Reduce the dosage of Clarithromycin by 50%
Patients with severe renal impairment (CL <sub>cr</sub> of <30 mL/min) taking concomitant atazanavir or ritonavir-containing regimens	Reduce the dosage of Clarithromycin by 75%

### Dosage Adjustment Due to Drug Interactions

Decrease the dose of Clarithromycin by 50 % when co-administered with atazanavir. Dosage adjustments for other drugs when co-administered with Clarithromycin may be recommended due to drug interactions.

#### **If you take more Clarithromycin Tablets than you should;**

If you have taken too much of Clarithromycin, contact your doctor or nearest hospital emergency department as soon as possible. Overdose can cause gastrointestinal discomfort and possibly other complaints.

#### **If you forget to take Clarithromycin Tablets**

If you forget to take a dose of Clarithromycin, take it as soon as you remember. If it is almost time for your next dose, do not take the missed dose and just carry on as before. Do not take a double dose to make up for a forgotten dose.

#### **If you stop taking Clarithromycin Tablets:**

It is important that you take your medicine in accordance with the doctor's instructions. Do not suddenly stop using Clarithromycin without discussing it first with your doctor. Otherwise symptoms may return.

**If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.**

#### 4. Possible side effects

Like all medicines, Clarithromycin tablets can cause side effects, although not everybody gets them.

Contact a doctor immediately if you experience the following

Serious adverse reactions:

- Acute Hypersensitivity Reactions
- QT Prolongation
- Hepatotoxicity
- Serious Adverse Reactions Due to Concomitant Use with Other Drugs
- *Clostridium difficile* Associated Diarrhea
- Exacerbation of Myasthenia Gravis

Contact a doctor immediately if you experience of severe acute hypersensitivity reactions, such as anaphylaxis, Stevens-Johnson Syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), Henoch-Schonlein purpura, and acute generalized exanthematous pustulosis.

#### **Most frequent adverse reactions for both adult and pediatric populations:**

- abdominal pain,
- diarrhea,
- nausea,
- vomiting
- dysgeusia
- dyspepsia,
- liver function test abnormal,
- anaphylactic reaction,
- candidiasis,
- headache,
- insomnia, and
- rash.

#### **List the most common adverse reactions for prophylaxis and treatment of mycobacterial infections and duodenal ulcer associated with H. pylori infection:**

- Abdominal pain
- Headache
- Diarrhea
- Dyspepsia
- Flatulence
- Nausea
- Vomiting
- Rash
- Special Senses
- Taste Perversion

### Changes in Laboratory Values:

WBC Count, SGOT, SGPT

### Treatment of Mycobacterial Infections

Nausea, vomiting, abdominal pain, diarrhea, rash, and asthenia

### Less Frequent Adverse Reactions Observed During Clinical Trials of Clarithromycin

Based on pooled data across all indications, the following adverse reactions were observed in clinical trials with clarithromycin at a rate less than 1%:

- *Blood and Lymphatic System Disorders:* Leukopenia, neutropenia, thrombocytopenia, eosinophilia
- *Cardiac Disorders:* Electrocardiogram QT prolonged, cardiac arrest, atrial fibrillation, extrasystoles, palpitations
- *Ear and Labyrinth Disorders:* Vertigo, tinnitus, hearing impaired
- *Gastrointestinal Disorders:* Stomatitis, glossitis, esophagitis, gastroesophageal reflux disease, gastritis, proctalgia, abdominal distension, constipation, dry mouth, eructation, flatulence
- *General Disorders and Administration Site Conditions:* Malaise, pyrexia, asthenia, chest pain, chills, fatigue
- *Hepatobiliary Disorders:* Cholestasis, hepatitis
- *Immune System Disorders:* Hypersensitivity
- *Infections and Infestations:* Cellulitis, gastroenteritis, infection, vaginal infection
- *Investigations:* Blood bilirubin increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, albumin globulin ratio abnormal
- *Metabolism and Nutrition Disorders:* Anorexia, decreased appetite
- *Musculoskeletal and Connective Tissue Disorders:* Myalgia, muscle spasms, nuchal rigidity
- *Nervous System Disorders:* Dizziness, tremor, loss of consciousness, dyskinesia, somnolence
- *Psychiatric Disorders:* Anxiety, nervousness
- *Renal and Urinary Disorders:* Blood creatinine increased, blood urea increased
- *Respiratory, Thoracic and Mediastinal Disorders:* Asthma, epistaxis, pulmonary embolism
- *Skin and Subcutaneous Tissue Disorders:* Urticaria, dermatitis bullous, pruritus, hyperhidrosis, rash maculo-papular

Adverse reactions reported in clinical trials

- Gastrointestinal Adverse Reactions
- All-Cause Mortality in Patients with Coronary Artery Disease 1 to 10 Years Following Clarithromycin Exposure

### Post-marketing Experience

The following adverse reactions have been identified during post-approval use of Clarithromycin.

- *Blood and Lymphatic System:* Thrombocytopenia, agranulocytosis



- *Cardiac*: Ventricular arrhythmia, ventricular tachycardia, torsades de pointes
- *Ear and Labyrinth*: Deafness was reported chiefly in elderly women and was usually reversible.
- *Gastrointestinal*: Pancreatitis acute, tongue discoloration, tooth discoloration was reported and was usually reversible with professional cleaning upon discontinuation of the drug.
- *Hepatobiliary*: Hepatic failure, jaundice hepatocellular. Adverse reactions related to hepatic dysfunction have been reported with clarithromycin.
- *Infections and Infestations*: Pseudomembranous colitis
- *Immune System*: Anaphylactic reactions, angioedema
- *Investigations*: Prothrombin time prolonged, white blood cell count decreased, international normalized ratio increased. Abnormal urine color has been reported, associated with hepatic failure.
- *Metabolism and Nutrition*: Hypoglycemia has been reported in patients taking oral hypoglycemic agents or insulin.
- *Musculoskeletal and Connective Tissue*: Myopathy rhabdomyolysis was reported and in some of the reports, clarithromycin was administered concomitantly with statins, fibrates, colchicine or allopurinol.
- *Nervous System*: Parosmia, anosmia, ageusia, paresthesia and convulsions
- *Psychiatric*: Abnormal behavior, confusional state, depersonalization, disorientation, hallucination, depression, manic behavior, abnormal dream, psychotic disorder. These disorders usually resolve upon discontinuation of the drug.
- *Renal and Urinary*: Nephritis interstitial, renal failure
- *Skin and Subcutaneous Tissue*: Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), Henoch-Schonlein purpura, acne, acute generalized exanthematous pustulosis
- *Vascular*: Hemorrhage

### **Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

### **5. How to store Clarithromycin Tablets**

Store Clarithromycin Tablets below 30°C

### **6. Contents of the pack and other information**

#### **What Clarithromycin Tablets contains**

Each film coated Tablet contains

Clarithromycin USP 500 mg

Colour: Quinoline Yellow lake & Titanium Dioxide BP

**The other ingredients**

Microcrystalline Cellulose, Maize Starch, Povidone (Kollidon 30), Sodium Starch Glycolate, Colloidal Silicon Dioxide, Croscarmellose Sodium, Talc, Magnesium Stearate, Hypromellose. - 50 Cps, Polyethylene Glycol 6000, Titanium Dioxide, Lake Quinoline Yellow(Quinoline Yellow), Dibutyl Phthalate

**What Clarithromycin Tablets looks like and contents of the pack**

Yellow coloured, capsule shaped, film coated tablets, plain on both sides

3 Blister strips (PV/PE/PVDC-Alu) of 4's packed in a carton. 5 such cartons are packed in an outer carton.

**Marketing authorisation holder:****Registered office**

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