AGOG Pharma Ltd.

(WHO - GMP CERTIFIED - GOVT RECOGNISED EXPORT HOUSE)

Regd. Office & Factory : Plot No. 33, Sector II, The Vasai Taluka Industrial Co-op. Estate Ltd. Gauraipada, Vasai (E), Dist. Thane - 401 208. INDIA.
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LEAFLET

Clarithromycin Tablets BP 250 mg / 500 mg

COMPOSITION:
Each film coated tablet contains:
Clarithromycin BP 250 mg / 500mg
Excipients ..... q.s.
Approved colour used

PHARMACOLOGICAL ACTION
Clarithromycin is a macrolide antibiotic. It exerts its antibacterial action by binding reversibly to the 50S ribosomal subunit of the 70S ribosome of sensitive microorganisms, thereby inhibiting bacterial RNA-dependent protein synthesis. The in vitro antibacterial spectrum of pathogens sensitive to clarithromycin includes: (in vitro sensitivity does not necessarily imply in vivo efficacy)
Streptococcus agalactiae, Streptococcus pyogenes, Streptococcus pneumoniae
Legionelle pneumophilia
Mycoplasma pneumoniae
Chlamydia trachomatis
Moraxella (Branhamella) catarrhalis
Haemophilus influenzae
Staphylococcus aureus (methicillin sensitive)
Helicobacter pylori
Mycobacterium avium, Mycobacterium kansasii, Mycobacterium chelonae, Mycobacterium intracellulare

Pharmacokinetics:
Clarithromycin is absorbed rapidly from the gastrointestinal tract after oral administration, but its bioavailability is reduced to 50 to 55% because of rapid first-pass metabolism. Peak plasma concentration occurs approximately 2 hours after administration. Clarithromycin may be given with or without food. Clarithromycin is metabolised by the liver to the active metabolite, 14-hydroxyclarithromycin, as well as to several other metabolites. Both clarithromycin and 14-hydroxyclarithromycin distribute widely throughout the body and achieve high intracellular concentrations. Tissue concentrations generally exceed serum concentrations. Clarithromycin does not achieve significant levels in the cerebrospinal fluid. Protein binding of Clarithromycin ranges from 40 to 70% and is concentration-dependent. The elimination half-lives of clarithromycin and 14-hydroxyclarithromycin are approximately 3 to 7 and 5 to 9 hours respectively. Longer half-lives are observed after larger doses. Clarithromycin is eliminated by renal and nonrenal routes. The amount of clarithromycin excreted unchanged in the urine ranges from 20 to 40%, depending on the dose administered and the formulation. Between 10 and 15% of the dose is excreted in the urine as the 14-hydroxy metabolite. Although the pharmacokinetics of clarithromycin are altered in patients with hepatic or renal dysfunction, dosage adjustment is not necessary unless a patient has severe renal dysfunction (creatinine clearance of <30 mL/minute). At higher doses in HIV-infected patients clarithromycin and 14-hydroxyclarithromycin concentrations are much higher when compared with usual doses in non-infected patients. The elimination half-lives also appear to be lengthened.

INDICATIONS:
Clarithromycin is indicated for the treatment of the following mild to moderate severe infections caused by susceptible organisms:
- Lower respiratory tract infections such as bronchitis and pneumonia.
- Upper respiratory tract infections such as pharyngitis and sinusitis.
- Mild to moderately severe acute otitis media due to S. pneumoniae, M. catarrhalis and H. influenza.
- Skin and soft tissue infections such as folliculitis, cellulitis or erysipelas.
- Eradication of Helicobacter pylori when used in combination with a proton pump inhibitor and another antibiotic to decrease recurrence of duodenal ulcer.

CONTRAINDICATIONS:
Clarithromycin 500 mg every 8 hours was given in combination with omeprazole 40 mg daily to healthy adult subjects. The steady-state plasma concentrations of omeprazole were increased (Cmax , AUC0-24 , and t½increases of 30%, 89%, and 34%, respectively), by the concomitant administration of clarithromycin. The mean 24-hour gastric pH value was 5.2 when omeprazole was administered alone and 5.7 when coadministered with clarithromycin.
Coadministration of clarithromycin with ranitidine bismuth citrate resulted in increased plasma ranitidine concentrations (57%), increased plasma bismuth trough concentrations (48%), and increased 14-hydroxy-clarithromycin plasma concentrations (31%). These effects are clinically insignificant.
Following administration of fluconazole 200 mg daily and clarithromycin 500 mg twice daily to 21 healthy volunteers, the steady-state clarithromycin Cminand AUC increased 33% and 18%, respectively. Steady-state concentrations of 14-OH clarithromycin were not significantly affected by concomitant administration of fluconazole. No dosage adjustment of clarithromycin is necessary when co-administered with fluconazole.

Drug Interactions:
Clarithromycin use in patients who are receiving theophylline may be associated with an increase of serum theophylline concentrations. Monitoring of serum theophylline concentrations should be considered for patients receiving high doses of theophylline or with baseline concentrations in the upper therapeutic range. In two

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studies in which theophylline was administered with clarithromycin (a theophylline sustained-release formulation was dosed at either 6.5 mg/kg or 12 mg/kg together with 250 or 500 mg q12h clarithromycin), the steady-state levels of Cmax , Cmin , and the area under the serum concentration time curve of theophylline increased about 20%.

Hypotension, bradyarrhythmias, and lactic acidosis have been observed in patients receiving concurrent verapamil, belonging to the calcium channel blockers drug class.

Concomitant administration of single doses of clarithromycin and carbamazepine has been shown to result in increased plasma concentrations of carbamazepine. Blood level monitoring of carbamazepine may be considered.

When clarithromycin and terfenadine were coadministered, plasma concentrations of the active acid metabolite of terfenadine were threefold higher, on average, than the values observed when terfenadine was administered alone. The pharmacokinetics of clarithromycin and the 14-OH-clarithromycin were not significantly affected by coadministration of terfenadine once clarithromycin reached steady-state conditions.

PREGNANCY AND LACTATION:

Safety and efficacy in pregnancy and lactation have not been established.
Clarithromycin is excreted in the breast milk.

ADVERSE EFECTS:

The most frequently reported events in adults taking clarithromycin tablets BP were diarrhea (3%), nausea (3%), abnormal taste (3%), dyspepsia (2%), abdominal pain/discomfort (2%), and headache (2%). In pediatric patients, the most frequently reported events were diarrhea (6%), vomiting (6%), abdominal pain (3%), rash (3%), and headache (2%). Most of these events were described as mild or moderate in severity. The most frequently reported events in adults taking were diarrhea (6%), abnormal taste (7%), and nausea (3%). Most of these events were described as mild.

Haematological:

•Less frequent: Leucopenia, thrombocytopenia

Cardiovascular

•QT prolongation, ventricular tachycardia, torsades de pointes Nervous system:

•Headache, anxiety, dizziness, insomnia, hallucinations, bad dreams, vertigo, tinnitus, disorientation, depersonalization, confusion, hearing loss, convulsionsEndocrine/Metabolic:

•Less frequent: HypoglycemiaGastrointestinal:

•Frequent:Nausea, vomiting, abdominal pain, abnormal taste, diarrheaLess frequent:Glossitis, stomatitis, oral candidiasis, tongue discolouration, tooth discolouration, pseudomembranous colitis (abdominal cramps or pain, tenderness, severe, watery diarrhoea which may also be bloody, fever)

Liver:

•Less frequent: Increased in liver enzymes, hepatocellular and/or cholestatic hepatitis (with or without jaundice), pancreatitis

DOSAGE

The recommended dose for children under 6 months is based upon a 7,5 mg/kg dose, administered twice daily. In patients with severe renal function impairment (creatinine clearance <30 mL/min), the dosage of Clarithromycin should be reduced by half.

Clarithromycin may be taken with or without meals and can be taken with milk.

Adults: 250 mg twice daily.

In more severe infections, the dosage may be increased to 500 mg twice daily.

Eradication of H. pylori

Adults: 500 mg twice daily, in combination with an appropriate antibiotic and an acid lowering agent, for 7 to 10 days.

The safety and efficacy of Clarithromycin in combination with proton-pump inhibitors other than omeprazole has not been established.

Atypical mycobacterial infections in HIV patients

Adults: 500 mg twice daily

Treatment of disseminated MAC infections in AIDS patients should continue as long as clinical and microbiological benefit is demonstrated. A decrease in efficacy has been noted in patients taking Clarithromycin for more than 12 weeks. Clarithromycin should be used in conjunction with other antimycobacterial agents.

Clarithromycin may be taken with or without meals.

STORAGE:

Store under normal storage conditions (15°C to 30°C).
Protect from light.

Keep all medicines out of reach of children.

PRESENTATION:

Clarithromycin Tablet: A bulk pack of 100 tablets / Pack of 14 tablets.

Manufactured in India by:
AGOG PHARMA LTD.
Plot No. 33, Sector II, The Vasai Taluka Indl.
Co-op. Estate Ltd., Vasai (E), Dist. Thane. INDIA.