

Noviclar

(Clarithromycin)

نوویکلار
(کلیئریترومائی سین)

COMPOSITION

Noviclar Tablets 250 mg
Each film-coated tablet contains
Clarithromycin (U.S.P.) 250 mg
Product Complies U.S.P. Specs.

Noviclar Tablets 500 mg
Each film-coated tablet contains
Clarithromycin (U.S.P.) 500 mg
Product Complies U.S.P. Specs.

Noviclar Suspension 125 mg / 5 ml
Each 5 ml contains
Clarithromycin granules (manufacturer specs) eq. to
Clarithromycin 125 mg.
Product Complies U.S.P. Specs.

DESCRIPTION

Clarithromycin is a semi-synthetic macrolide antibiotic obtained by substitution of the hydroxyl group in position 6 by a CH₃O group in the erythromycin lactonic ring. Specifically clarithromycin is 6-O-Methyl Erythromycin A.

CLINICAL PHARMACOLOGY

Microbiology
Clarithromycin exerts its antibacterial action by binding to the 50S ribosomal subunits of susceptible bacteria and suppressing protein synthesis.

Clarithromycin has been shown to be active against most strains of the following micro-organisms both *in vitro* and in clinical infections as described in the indications and usage section:

The *in vitro* antibacterial spectrum of clarithromycin is as follows.

Aerobic Gram-Positive microorganisms
Staphylococcus aureus
Streptococcus pneumoniae
Streptococcus pyogenes
Listeria monocytogenes

Aerobic Gram-negative microorganisms
Haemophilus influenzae
Haemophilus parainfluenzae
Moraxella catarrhalis
Neisseria gonorrhoeae
Legionella pneumophila

Other microorganisms
Mycoplasma pneumoniae
Chlamydia pneumoniae (TWAR)

Mycobacteria
Mycobacterium leprae
Mycobacterium kansasii
Mycobacterium chelonae
Mycobacterium fortuitum
Mycobacterium avium complex (MAC) consisting of:
Mycobacterium avium
Mycobacterium intracellulare

Beta-lactamase production should have no effect on

clarithromycin activity.

NOTE: Most strains of methicillin-resistant and oxacillin-resistant staphylococci are resistant to clarithromycin.

Helicobacter
Helicobacter pylori

The following *in vitro* data are available, but their clinical significance is unknown. Clarithromycin exhibits *in vitro* activity against most strains of the following microorganisms; however the safety and effectiveness of clarithromycin in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

Aerobic Gram-positive microorganisms
Streptococcus agalactiae
Streptococci (Group C,F,G)
viridans group streptococci

Aerobic Gram-negative microorganisms
Bordetella pertussis
Pasteurella multocida

Anaerobic Gram-positive microorganisms
Clostridium perfringens
Peptococcus niger
Propionibacterium acnes

Anaerobic Gram-negative microorganisms
Bacteroides melaninogenicus

Spirochetes
Borrelia burgdorferi
Treponema pallidum
Campylobacter
Campylobacter jejuni

Pharmacokinetics

The kinetics of orally administered clarithromycin has been studied extensively in a number of animal species and adult humans. These studies have shown clarithromycin is readily and rapidly absorbed with an absolute bioavailability of approximately 50%. Little or no unpredicted accumulation was found and the metabolic disposition did not change in any species following multiple dosing. Food intake immediately before dosing increases clarithromycin bioavailability by a mean of 25%. Overall, this increase is minor and should be of little clinical significance with the recommended dosing regimens. Clarithromycin may thus be administered in either the presence or absence of food.

INDICATIONS

Clarithromycin is indicated for treatment of infections due to susceptible organisms. Such infections include:

1. Lower respiratory tract infections (e.g., bronchitis, pneumonia)
2. Upper respiratory tract infections (e.g., pharyngitis, sinusitis);
3. Acute otitis media.
4. Skin and soft tissue infections (e.g., folliculitis, cellulitis, erysipelas);
5. Disseminated or localized mycobacterial infections due to *Mycobacterium avium* or *Mycobacterium intracellulare*. Localized infections due to *Mycobacterium chelonae*, *Mycobacterium fortuitum*, or *Mycobacterium kansasii*;
6. Clarithromycin is indicated for the prevention of disseminated *Mycobacterium avium* complex infection in HIV-infected patients with CD4 lymphocyte counts

less than or equal to 100/mm³;

7. Clarithromycin in the presence of acid suppression is also indicated for the eradication of *H. pylori* resulting in decreased recurrence of duodenal ulcer (see FURTHER INFORMATION).
8. Treatment of odontogenic infections.

CONTRAINDICATIONS

Clarithromycin is contraindicated in patients with known hypersensitivity to macrolide antibiotic drugs.

Concomitant administration of clarithromycin and any of the following drugs is contraindicated: astemizole, cisapride, pimozide, and terfenadine (see PRECAUTIONS - Drug Interactions).

WARNING

The physician should not prescribe clarithromycin to pregnant women without carefully weighing the benefits against risk, particularly during the first 3 months of pregnancy.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including macrolides, and may range in severity from mild to life-threatening.

PRECAUTIONS

Clarithromycin is principally excreted by the liver. Therefore, caution should be exercised in administering the antibiotic to patients with impaired hepatic function. Caution should also be exercised when administering clarithromycin to patients with moderate to severe renal impairment. Attention should also be paid to the possibility of cross resistance between clarithromycin and other macrolide drugs, as well as lincomycin and clindamycin.

Drug interactions

Cytochrome P450 Interactions

Data available to date indicate clarithromycin is metabolized primarily by the hepatic cytochrome P450 3A (CYP3A) isozyme. This is an important mechanism determining many drug interactions. The metabolism of other drugs by this system may be inhibited by concomitant administration with clarithromycin and may be associated with elevations in serum levels of these other drugs.

The following drugs or drug classes are known or suspected to be metabolized by the same CYP3A isozyme: alprazolam, astemizole, carbamazepine, clobazepam, cisapride, cyclosporine, disopyramide, ergot alkaloids, lovastatin, methylprednisolone, midazolam, omeprazole, oral anticoagulants (e.g. warfarin), pimozide, quinine, rifabutin, sildenafil, simvastatin, tacrolimus, terfenadine, triazolam, and vinblastine. Drugs interacting by similar mechanisms through other isozymes within the cytochrome P450 system include phenytoin, theophylline and valproate. Results of clinical studies indicate there was a modest but statistically significant (P ≤ 0.05) increase of circulating theophylline or carbamazepine levels when either of these drugs are administered concomitantly with clarithromycin.

Usage During Pregnancy And Lactation

The safety of clarithromycin for use during pregnancy and breast feeding of infants has not been established. Clarithromycin is excreted into human breast milk.

ADVERSE REACTIONS

The most frequently reported side effects of clarithromycin in clinical studies in adults were gastrointestinal-related complaints, i.e., nausea, dyspepsia, abdominal pain, vomiting and diarrhea. Other side effects included headache, taste perversion, and transient elevations of liver enzymes.

FURTHER INFORMATION

Helicobacter pylori is strongly associated with peptic ulcer disease. Ninety (90) to 100% of patients with duodenal ulcer are infected with this pathogen. Eradication of *H. pylori* has been shown to reduce the rate of duodenal ulcer recurrence, thereby reducing the need for maintenance anti-secretory therapy.

Triple Therapy in Duodenal Ulcer Disease

In a well controlled double blind study, *H. pylori* infected duodenal ulcer patients received triple therapy with clarithromycin 500 mg BID, amoxicillin 1000 mg BID and omeprazole 20 mg daily for 10 days or dual therapy with clarithromycin 500 mg TID and omeprazole 40 mg daily for 14 days. *H. pylori* was eradicated in 90% of the patients receiving clarithromycin triple therapy and in 60% of the patients receiving dual therapy.

In an independent study *H. pylori* infected patients received eradication therapy with clarithromycin 500 mg BID in conjunction with amoxicillin 1000 mg BID and omeprazole 20 mg qd (Group A) or omeprazole 20 mg BID (Group B) for 7 days. In those patients not previously treated with anti-*H. pylori* therapy, *H. pylori* was eradicated in 88% of patients in Group A and 86% of patients in Group B.

In an open-label study *H. pylori* infected patients with duodenal ulcer or non ulcer dyspepsia (NUD) received eradication therapy with clarithromycin 500 mg bid, lansoprazole 30 mg bid plus amoxicillin 1000 mg bid for 10 days. In all-patients-treated analysis, *H. pylori* was eradicated from 91% of patients.

Dual Therapy in Duodenal Ulcer Disease

In Well controlled, double-blind studies, *H. pylori* infected duodenal ulcer patients received eradication therapy with clarithromycin 500 mg TID and omeprazole 40 mg daily for 14 days followed by omeprazole 40 mg (study A) or omeprazole 20 mg (studies B, C and D) daily for an additional 14 days; patients in each control group received omeprazole alone for 28 days. In study A, *H. pylori* was eradicated in over 80% of patients who received clarithromycin and omeprazole and in only 1% of patients receiving omeprazole alone. In studies B, C, and D, the combined eradication rate was over 70% in patients receiving clarithromycin and omeprazole and less than 1% in patients receiving omeprazole alone. In each study, the rate of ulcer recurrence at 6 months was statistically lower in the clarithromycin and omeprazole treated patients when compared to patients receiving omeprazole alone.

In an investigator-blind study, *H. pylori* infected patients received eradication therapy with clarithromycin 500 mg TID in conjunction with lansoprazole 60 mg/day in single or divided doses for 14 days. The combined eradication rate was over 60%.

DOSAGE AND ADMINISTRATION

The usual recommended dosage of clarithromycin in adults is one 250 mg tablet twice daily. In more severe infections, the dosage can be increased to 500 mg twice daily. The usual duration of therapy is 5 to 14 days, excluding treatment of commonly acquired pneumonia and sinusitis which require 6 to 14 days of therapy.

The recommended daily dosage of Noviclar Pediatric Suspension (125mg/5mL) in children is 7.5 mg/kg BID up

to maximum dose of 500mg BID fro non-mycobacterial infections. The usual duration of treatment is for 5 to 10 days depending on the pathogen involved and the severity of the condition. The prepared suspension can be taken with or without meals, and can be taken with milk.

DOSAGE GUIDELINES FOR PEDIATRIC PATIENTS Based on Body Weight			
Weight*		Dosage in Standard 5mL Teaspoonful given twice daily	
Kg	Lbs.	125 mg/5 mL	
8-11	18-25	0.5	
12-19	26-43	1	
20-29	44-64	1.5	
30-40	65-88	2	

* Children <8kg / <18 lbs. should be dosed on a per kg on per lb. basis (approx. 7.5 mg/kg BID or 3.4 mg/lb BID)

In patients with renal impairment with creatinine clearance less than 30 mL/min, the dosage of clarithromycin should be reduced by one-half, i.e., 250 mg once daily, or 250 mg twice daily in more severe infections. Treatment should not be continued beyond 14 days in these patients.

Dosage in patients with mycobacterial infections: The recommended dose for adults with mycobacterial infections is 500 mg BID.

In children with disseminated or localized mycobacterial infections (M. avium, M. intracellulare, M. chelonae, M. fortuitum, M. kansasii), the recommended dose is 15 to 30 mg/kg clarithromycin per day in two divided doses.

Treatment of disseminated MAC infections in AIDS patients should be continued, as long as clinical and microbiological benefit is demonstrated. Clarithromycin should be used in conjunction with other antimycobacterial agents.

Treatment of other nontuberculous mycobacterial infections should continue at the discretion of the physician.

Dosage for MAC prophylaxis: The recommended dosage of clarithromycin in adults is 500 mg twice daily.

In the treatment of odontogenic infections, the dosage of clarithromycin is one 250 mg tablet twice daily for 5 days.

Triple Therapy Regimen

Clarithromycin 500 mg b.i.d in conjunction with pantoprazole 40 mg bid plus amoxicillin 1000 mg bid for seven to ten days.

Clarithromycin 500 mg b.i.d in conjunction with lansoprazole 30 mg bid plus amoxicillin 1000 mg bid for 10 days.

Clarithromycin 500 mg b.i.d in conjunction with omeprazole 20 mg bid plus amoxicillin 1000 mg bid for seven to ten days.

Dual Therapy Regimens

Clarithromycin 500 mg t.i.d in conjunction with omeprazole 40 mg daily for 14 days, followed by omeprazole 20 mg or 40 mg daily for an additional 14 days.

Clarithromycin 500 mg TID in conjunction with lansoprazole

60 mg daily for 14 days. Further acid suppression may be required to complete ulcer healing.

DIRECTION FOR PREPARATION OF SUSPENSION

Prepare Suspension according to the instructions given on the label.

NOTE: After preparation, the suspension may be kept for 14 days without significant loss of potency. Do not refrigerate the reconstituted suspension.

HOW SUPPLIED

Noviclar film coated tablets 250 mg is supplied in blister of 10's in carton.

Noviclar film coated tablets 500 mg is supplied in blister of 10's in carton.

60 ml oral suspension (after reconstitution) in the bottle containing 125 mg / 5 mL.

STORAGE

Store below 30°C in a dry place, protect from light. Keep bottle tightly closed. To be dispensed on the prescription of a registered medical practitioner only. Keep out of the reach of children.

دوا تیار کرنے کا طریقہ:

لیبل پر دی گئی ہدایت کے مطابق تیار کریں۔

نوٹ: پانی مانے کے بعد ۱۵ دن تک دوا کی اصل تاثیر برقرار رہتی ہے

تیار شدہ دوا ریفریجریٹر میں نہ رکھیں۔

استعمال سے پہلے دوا کو اچھی طرح ہلا لیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر

خشک جگہ پر رکھیں۔ دھکن کو اچھی طرح بند رکھیں۔ صرف رجسٹرڈ

ڈاکٹر کے نسخے پر فروخت کریں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:

Platinum
Pharmaceuticals (Pvt) Ltd.

A-20, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

QAR No. AW21-0740