CLITH-500

Cautions:
Clith-500 is primarily excreted by the liver hence caution should be exercised in administering the antibiotic in the presence of impaired hepatic function.
Pseudomembranous colitis is possible and may range in severity from mild to life-threatening.
There is possible cross resistance between Clith-500 and other macrolides, as well as Lincomycin and Clindamycin.

Dose:
Recommended dosage is 250-500mg to be taken twice daily, depending on severity of infection.
In renal impairment, dose should be reduced to 250mg once or twice daily and treatment should not go beyond 14 days in these patients.
Eradication of *H.pylori*: Clith-500 to be given twice daily in combination with 1g Amoxicillin twice daily and Omeprazole 20mg daily for 7-10 days.

Adverse effects:
Most common adverse effects are gastrointestinal-related, such as nausea, dyspepsia, abdominal pain, vomiting and diarrhoea. Tooth and reversible tongue discolouration has been observed. Other side effects include headache and skin rash.
Hepatic dysfunction, usually reversible, including raised liver enzymes, and hepatocellular and/or cholestatic hepatitis has been infrequently reported with Clarithromycin. Treatment with Clith-500 should be discontinued if any signs of hepatic dysfunction develop.
Rarely hypoglycaemia occurs, some occurring in patients on concomittant oral hypoglycaemic agents or insulin.

There are some rare cases of thrombocytopenia and allergic reactions are also possible ranging from mild skin eruptions to anaphylaxis and Steven-Johnson Syndrome. There have been reports of transient central nervous system side effects including anxiety, dizziness, insomnia, hallucinations, convulsions, psychosis; however, a cause and effect relationship has not been established.
There is possible hearing loss that is reversible on withdrawal of therapy. Also there is a possibility of ventricular arrhythmias including ventricular tachycardia, and torsade de pointes in individuals with prolonged QT intervals.
Glossitis, stomatitis, oral moniliasis have been reported with Clarithromycin therapy.

Interactions:
There is a modest but significant increase in Theophylline or Carbamazepine levels when concomitantly administered with Clith-500.
Elevated levels of Cisapride and Pimozide have also been reported.
Clith-500 may potentiate the effects of Warfarin; prothrombin times should be monitored in these patients.
Decreased serum of Clarithromycin have been reported when co-administered with Nevirapine due to enzyme induction by Nevirapine.
The use of Clith-500 in patients concurrently taking drugs metabolized by the cytochrome P450 enzymes such as Warfarin, ergot alkaloids, Triazolam, Midazolam, Phenytoin, Cyclosporin may be associated with elevations in serum levels of these other drugs.
Elevated Digoxin levels have been reported when taken concomitantly with Clith-500. Monitoring of Digoxin levels should be considered.
Clith-500 may alter the metabolism of Terfenadine resulting in increased levels of Terfenadine which has occasionally been associated with cardiac arrhythmias such as QT prolongation, ventricular tachycardia, ventricular fibrillation and torsade de pointes. Similar effects have been observed in patients taking Clarithromycin and Astemizole.
Simultaneous oral administration of Clarithromycin and Zidovudine may result in decreased steady-state Zidovudine concentrations by interfering with its absorption. This interaction can be avoided by staggering the dose of Zidovudine and Clith-500.
Ritonavir inhibits the metabolism of Clarithromycin. Because of the large therapeutic window of Clarithromycin, no dosage reduction is necessary in patients with normal renal function.

Overdose:
Ingestion of large amounts of Clith-500 can be expected to produce gastrointestinal symptoms. Allergic reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug and supportive measures. Clith-500 serum levels are not expected to be appreciably affected by haemodialysis or peritoneal dialysis.

Presentation:
Clith-500 is supplied in blister packs of 10's, 20's, 40's, 100's in unit boxes and 500's & 1000's in plastic securitainer containers.

Storage:
Do not store above 30°C. Store in a dry place. Protect from direct sunlight. Keep all medicines out of reach of children.

Manufactured by:

UNIVERSAL
CORPORATION LTD.
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CLITH-500

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Medium and broad spectrum macrolide antibiotic.

Composition:
Each Clith-500 tablet contains 500mg Clarithromycin B.P.

Identification:
Pale yellow film coated tablet scored on one side, plain on the reverse side.

Pharmacology:
Clith-500 exerts its antibacterial action by binding to the 50S ribosomal subunits of susceptible bacteria and thereby suppressing protein synthesis. In vitro sensitivity does not necessarily imply in vivo efficacy. The in vitro antibacterial spectrum of pathogens usually sensitive to Clith-500 includes *Streptococcus agalactiae, Streptococcus pyogenes, Streptococcus pneumoniae, Legionella pneumoniae, Mycoplasma pneumoniae, Chlamydia trachomatis, Branhamella catarrhalis, certain strains of Staphylococcus aureus, Haemophilus influenzae, Helicobacter (Campylobacter) pylori, Mycobacterium avium, Mycobacterium kansasii, Mycobacterium chelonae, Mycobacterium intracellulare.* Clith-500 is bactericidal to *Helicobacter pylori*, this activity being greater at neutral pH than at acid pH. The 14-hydroxy-clarithromycin metabolite also has antibacterial activity.

Pharmacokinetics:
Mean plasma peak levels after a single oral dose of Clith-500 occur approximately 2 hours after administration and range from 0.35µg/ml after a 100mg dose to 3.97µg/ml after a 1200mg dose. Mean half-life appears to be dose-dependent and ranges from 2.27 hours after a 100mg dose to 5.98 hours after the 1200mg dose. Results of a study of the effects of food on absorption indicated that food taken shortly before dosing somewhat delayed the onset of absorption of Clarithromycin. However, food intake did not affect the overall bioavailability of the drug. Protein binding decreases with increasing drug concentration in the plasma. The average percentage binding of Clarithromycin was 70% for plasma concentrations of 0.45-4.5µg/ml and 41% for plasma concentrations of 45µg/ml. Thus 14C-Clarithromycin is not extensively bound to plasma proteins and its binding sites appear to be readily saturated at high drug concentrations.
Clarithromycin and its 14-OH-metabolite distribute readily into body tissues and fluids. Limited data from a small number of patients suggests that Clarithromycin does not achieve significant levels in cerebrospinal fluid after oral doses; only 1-2% of serum levels in CSF in patients with normal blood-cerebrospinal fluid barriers. Concentrations in tissues are higher than serum concentrations.
The major metabolite in plasma is the 14-hydroxy(R) epimer of Clarithromycin. Low levels are also seen in plasma of descaldinosyl-clarithromycin only after a 1200mg dose. The non-linear pharmacokinetic behaviour of Clarithromycin, coupled with the overall decrease in the formation of 14-hydroxylation and N-demethylation products at the higher doses, indicate that metabolism of Clarithromycin approaches saturation at high doses.
With single oral doses of 250mg or 1200mg Clarithromycin, urinary excretion accounted for 37.9% of the lower dose and 46% of the higher dose, the parent drug and 14-hydroxy Clarithromycin accounting for most of it. Comparison of the metabolic profiles in urine and faeces indicated that the products of secondary metabolism were excreted primarily in the faeces.
Steady state concentrations of Clarithromycin and 14-OH-clarithromycin observed following administration of usual doses to adult patients with HIV infection were similar to those observed in normal subjects. However, at the higher doses which may be required to treat mycobacterial infections, Clarithromycin concentrations were much higher than those observed at the usual doses. In adult HIV-infected patients taking 1000 and 2000mg/day in two divided doses, steady-state Clarithromycin Cmax values ranged from 2-4µg/ml to 5-10µg/ml respectively. Elimination half-lives appeared to be lengthened at these higher doses as compared to those seen with usual doses in normal subjects.

Indications:
Upper and lower respiratory tract infections, such as bronchitis, pneumonia, pharyngitis, sinusitis.
Skin and soft tissue infections like folliculitis, cellulitis, erysipelas.
Treatment of *H. pylori*; decreasing recurrence of duodenal ulcer when used in combination of proton pump inhibitor and another antibiotic.
Disseminated and localized infections in HIV-positive adults, due to *Mycobacterium avium* or *Mycobacterium intracellulare* respond to Clarithromycin in conjunction with other antimycobacterials. To a lesser extent, localized infections due to *Mycobacterium chelonae* and *Mycobacterium kansasii* have responded to Clarithromycin.

Contraindications:
Clith-500 is contraindicated in patients with known hypersensitivity to macrolide antibiotics.
Clith-500 should not be co-administered with Cisapride, Pimozide and Terfenadine.

Pregnancy and lactation:

There is not enough data to establish safety in pregnancy and lactation. Clith-500 is excreted in breast milk. Its administration in these special cases should hence be on the advice of your physician.