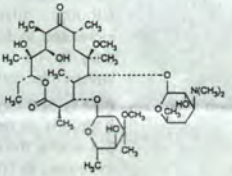
CLERON

Cleron tablets 250mg: 14's
Cleron tablets 500mg: 14's

DESCRIPTION: Cleron tablets contain clarithromycin



ACTIONS: Cleron is a semi-synthetic macrolide antibiotic. Its antibacterial action results from its binding to the 50s ribosomal subunit of susceptible bacteria, thus suppressing protein synthesis.

INDICATIONS: Cleron is indicated for the treatment of mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

Upper respiratory tract infections
Pharyngitis/Tonsillitis due to Streptococcus pyogenes

Acute maxillary sinusitis due to Streptococcus pneumoniae

Lower respiratory tract infections
Acute bacterial exacerbation of chronic bronchitis due to Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae.

Pneumonia due to Mycoplasma pneumoniae, or Streptococcus pneumoniae.

Skin Structure and Soft Tissue Infections due to Staphyloccocus aureus, or Streptococcus pyogenes. Abscesses usually require surgical drainage.

Cleron is indicated for the treatment of disseminated mycobacterial infections due to Mycobacterium avium, Mycobacterium intracellulare, Mycobacterium chelonae and Mycobacterium fortuitum.

Cleron is indicated for the eradication of Helicobacter pylori in the treatment of ulcer, provided that it is administered in conjuction with an agent which inhibits gastric acid.

CONTRAINDICATIONS: Patients with a known hypersensitivity to Cleron or any of the macrolide antibiotics.

PHARMACOKINETICS AND PHARMACOLOGY: Clarithromycin is rapidly absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability of 250-mg clarithromycin tablets was approximately 50%. Food slightly delays both the onset of clarithromycin absorption and the formation of the antimicrobially active metabolite, 14-OH clarithromycin, but does not affect the extent of bioavailability. Therefore, CLERON tablets may be given without regard to food.

In fasting healthy human subjects, peak serum concentrations were attained within 2 hours after oral dosing. Steady-state peak serum clarithromycin concentrations were attained in 2 to 3 days and were approximately 1μg/mL with a 250-mg dose administered every 12 hours, 2 to 3 μg/mL with a 500-mg dose administered every 12 hours, and 3 to 4 μg/mL with a 500mg dose administered every 8 hours. The elimination half-life of clarithromycin was about 3 to 4 hours with 250 mg administered every 12 hours but increased to 5 to 7 hours with 500 mg administered every 8 to 12 hours. The nonlinearity of clarithromycin pharmacokinetics is slight at the recommended doses of 250 mg and 500 mg administered every 8 to 12 hours. With a 250 mg every 12 hours dosing, the principal metabolite, 14-OH clarithromycin, attains a peak steady-state concentration of about 0.6 μg/mL and has an elimination half-life of 5 to 6 hours. With a 500 mg every 8 to 12 hours dosing, the peak steady-state concentration of 14-OH clarithromycin is slightly higher (up to 1μg/mL), and its elimination half-life is about 7 to 9 hours. With any of these dosing regimens, the steady-state concentration of this metabolite is generally attained within 2 to 3 days.

After a 250-mg tablet every 12 hours, approximately 20% of the dose is excreted in the urine as clarithromycin, while after a 500-mg tablet every 12 hours, the urinary excretion of clarithromycin is somewhat greater, approximately 30%. In comparison, after an oral dose of 250 mg (125 mg/5 mL) suspension every 12 hours, approximately 40% is excreted in urine as clarithromycin. The renal clearance of clarithromycin is, however, relatively independent of the dose size and approximates the normal glomerular filtration rate. The major metabolite found in urine is 14-OH clarithromycin, which accounts for an additional 10% to 15% of the dose with either a 250-mg or a 500-mg tablet administered every 12 hours.

WARNINGS AND PRECAUTIONS: Cleron is principally excreted via the liver and kidneys. Caution should be exercised in patients with impaired renal or hepatic function.

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

INTERACTIONS: Cleron use in patients who are receiving theophylline may be associated with an increase of serum theophylline concentrations.

Single-dose administration of Cleron has been shown to result in increased concentrations of carbamazepine.

Blood level monitoring of carbamazepine may be considered.

When Cleron and terfenadine were co-administered, plasma concentrations of the active acid metabolite of terfenadine, were three-fold higher, on average, than the values observed when terfenadine was administered alone.

Simultaneous oral administration of Cleron and zidovudine to HIV-infected adult patients resulted in decreased steady-state zidovudine concentration.

Cleron use in patients who are receiving warfarin may result in a potentiation of the effects of warfarin.

The effects of digoxin may be potentiated with concomitant use of Cleron.

PREGNANCY AND LACTATION: Pregnancy category C. There are no adequate and well-controlled studies in pregnant women. Cleron should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus.

It is not known whether Cleron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Cleron is administered to a nursing woman.

ADVERSE REACTIONS: Cleron is generally well tolerated. Side-effects include nausea, vomiting, diarrhoea and abdominal pain. Stomatitis and glossitis have been reported. Other side-effects include headache and allergic reactions ranging from urticaria and mild skin reactions to anaphylaxis. Taste perversion may occur. There have been reports of transient central nervous system side effects including anxiety, dizziness, insomnia, hallucinations, bad dreams and confusion, however, a cause and effect relationship has not been established.

DOSAGE AND ADMINISTRATION: Cleron may be given without regard to meals as food does not affect the extent of bioavailability.

Adults, children over 12 years old and elderly:	The usual dose is 250 mg twice daily for 7 days although this may be increased to 500 mg twice daily for up to 14 days in severe infections.
Mycobacterium infections:	Initially 500 mg twice daily. If there is no response after 3-4 weeks, the dose may be increased to 1000 mg twice daily, for as long as there is clinical improvement.
Eradication of H. pylori:	500 mg, three times daily, for 14 days.

Renal impairment: Dosage adjustments are not usually required except in patients with severe renal impairment (creatinine clearance < 30 ml/min).
If adjustment is necessary, the total daily dosage should be reduced by half, e.g. 250 mg once daily or 250 mg twice daily in more severe infections.

OVERDOSAGE: Reports indicate that the ingestion of large amounts of Cleron can be expected to produce gastro-intestinal symptoms. Allergic reactions accompanying overdosage should be treated by gastric lavage and supportive measures.

STORAGE: Store in a dry place protected from light, below 25°C.