CLARITEK

[Clarithromycin Tablets USP 250mg & 500mg]
[Clarithromycin Oral Suspension USP 125mg / 5mL]

DESCRIPTION
Clarithromycin is a semi-synthetic macrolide antibiotic obtained by substitution of the hydroxyl group in position 6 by a CH₂ group in the erythromycin lactonic ring. Chemically clarithromycin is 6-O-Methylerythromycin. The molecular formula is C₃₅H₆₇NO₁₄ and the structural formula is:

![Clarithromycin Structural Formula]

QUALITATIVE & QUANTITATIVE COMPOSITION
CLARITEK (Clarithromycin) is available as film-coated tablets and oral suspension:

1. CLARITEK Tablets 250mg Each tablet contains:
   Clarithromycin USP .... 250mg

2. CLARITEK Tablets 500mg Each tablet contains:
   Clarithromycin USP .... 500mg

3. CLARITEK Drops 125mg/5mL (25mL)
   Each reconstituted 5mL contains:
   Clarithromycin USP .... 125mg

4. CLARITEK Granules 125mg/5mL (10mL)
   Each reconstituted 5mL contains:
   Clarithromycin USP .... 125mg

CLINICAL PHARMACOLOGY
Mechanism of Action
Clarithromycin exerts its antibacterial action by binding to the 50S ribosomal subunits of susceptible bacteria and suppresses protein synthesis. Clarithromycin has demonstrated excellent in vitro activity against both standard strains of bacteria and clinical isolates. It is highly potent against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms. The minimum inhibitory concentrations (MICs) of clarithromycin are generally one log dilution more potent than the MICs of erythromycin.

Clarithromycin is reported to be more active than erythromycin against susceptible streptococci and staphylococci in vitro, as well as against some other species including Moraxella catarrhalis (Branhamella catarrhalis), Legionella spp., Clostridium botulinum, and Ureaplasma urealyticum. Clarithromycin is reported to be more active than erythromycin or azithromycin against some mycobacteria, including Mycobacterium avium complex, M. leprae, and against L. pneumophila and P. aeruginosa. It is active against H. pylori. It is less active in vitro against the proteus (Proteus vulgaris) group, and may have some activity against Escherichia coli and enterococci. It has been shown to enhance the activity of clindamycin in vivo, notably against Peptostreptococcus necrophorum. In vitro data also indicate that clarithromycin has less activity against Listeria pneumophila, and Pseudomonas pneumoniae. It is bactericidal to Helicobacter pylori. This activity of clarithromycin is greater at neutral pH than at acid pH. In vivo and in vivo data show that this antibiotic has activity against clinically significant mycobacterial species.

PHARMACOKINETICS
Absorption:
Clarithromycin is rapidly absorbed from the GI tract after oral administration and the bioavailability of the parent drug is about 55%. Food slightly delays the absorption of clarithromycin but does not effect the extent of bioavailability, therefore it may be given without regard to food. Peak concentrations of clarithromycin and its principal metabolite 14-hydroxyclarithromycin are excreted in urine; at steady state about 20% and 30% of a 250mg or 500mg dose, respectively, is excreted in this way, as unchanged drug. 14-hydroxyclarithromycin amounts are excreted in urine; at steady state about 20% and 30% of a 250mg or 500mg dose, respectively, is excreted in this way, as unchanged drug. The pharmacokinetics of clarithromycin is non-linear and dose dependent; high doses given without regard to food. Peak concentrations of clarithromycin and its principal metabolite 14-hydroxyclarithromycin are much higher than those observed at usual doses. In children with HIV infection taking 15-30mg/kg/day of clarithromycin in two divided doses, steady-state Cmax values generally ranged from 8 to 20mcg/mL. However, Cmax values as high as 24mcg/mL have been observed in HIV-infected pediatric patients taking 30mg/kg/day in two divided doses as clarithromycin pediatric suspension. Elimination half-lives appeared to be lengthened at these higher doses as compared to that observed with usual doses in normal subjects. The higher plasma concentrations and longer elimination half-lives observed at these doses are consistent with the known nonlinearity in clarithromycin pharmacokinetics.

THERAPEUTIC INDICATIONS
CLARITEK (Clarithromycin) is indicated for treatment of infections due to susceptible organisms. Such infections include:

- Lower respiratory tract infections (e.g., bronchitis, pneumonia)
- Upper respiratory tract infections (e.g., pharyngitis, sinusitis, tonsillitis)
- Acute otitis media in children
- Skin and soft tissue infections (e.g., folliculitis, cellulitis, erysipelas)
- Leprosy
- Disseminated or localized mycobacterial infections due to Mycobacterium avium or Mycobacterium intracellulare
- Localized infections due to Mycobacterium chelonae, Mycobacterium fortuium, or Mycobacterium kansasii
- It is also used in some countries as an alternative to pentamidine for prophylaxis of Pneumocystis carinii pneumonia
- To eradicate Helicobacter pylori in treatment regimens for peptic ulcer disease. It has been tried in protocol infections, including bronchopneumonia.
- Clarithromycin tablets and granules for oral suspension are indicated for the prevention and treatment of Mycobacterium avium complex (MAC) disease in patients with advanced HIV infection.

DOSE AND ADMINISTRATION
Adults:
The usual recommended dosage of CLARITEK (Clarithromycin) is one 250mg tablet twice daily. In more severe infections, the dosage can be increased to 500mg twice daily. The usual duration of therapy is 7 to 14 days. CLARITEK (Clarithromycin) suspension may be used as an alternative dosage form for those adults that prefer a liquid medicine.

The following table is a suggested guide for determining dosage.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Dosage (mg)</th>
<th>Normal Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis/Tonsillitis</td>
<td>250mg</td>
<td>10</td>
</tr>
<tr>
<td>Acute maxillary sinusitis</td>
<td>250mg</td>
<td>10</td>
</tr>
<tr>
<td>Acute exacerbation of chronic bronchitis due to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. pneumonia</td>
<td>250mg</td>
<td>10 to 14</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>250mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>MRSA</td>
<td>250mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Pneumonia due to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. pneumonia</td>
<td>250mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>M. pneumonia</td>
<td>250mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Uncomplicated skin and skin structure</td>
<td>250mg</td>
<td>7 to 14</td>
</tr>
</tbody>
</table>

Children:
The usual recommended daily dosage of CLARITEK (Clarithromycin) is 5mg/kg/day up to a maximum of 500mg twice daily. The usual duration of treatment is 5 to 10 days depending on the pathogen involved and the severity of the condition.
The following table is a suggested guide for determining dosage.

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Clarithromycin 250mg daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-15</td>
<td>625mg (1/2 tsp) 1250mg (2 tsp)</td>
</tr>
<tr>
<td>16-20</td>
<td>750mg (1 1/2 tsp) 1500mg (3 tsp)</td>
</tr>
</tbody>
</table>

Dosage in mL given twice daily (Clarithromycin 125mg/5mL)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Dosage in mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-15</td>
<td>2mL (1/4 tsp) 4mL (1/2 tsp)</td>
</tr>
<tr>
<td>16-20</td>
<td>3mL (1/2 tsp) 6mL (1 tsp)</td>
</tr>
</tbody>
</table>

Pregnancy and Lactation:
Clarithromycin is secreted into human breast milk therefore clarithromycin should not be used during pregnancy and breast-feeding unless the potential benefit justifies a potential risk to the fetus.

Drug Interactions:

- Antibiotic drugs.
- Clarithromycin is contraindicated in patients with known hypersensitivity to macrolide antibiotics and either a proton pump inhibitor or a histamine H₂-receptor antagonist.

Concomitant administration of clarithromycin with any of the following medicines is recommended:

- Clarithromycin should be given at least 2 hours before or 6 hours after administration of any of the above medicines.

Contraindications:
Clarithromycin is contraindicated in patients with known hypersensitivity to macrolide antibiotics.

Concomitant administration of clarithromycin with any of the following medicines is contraindicated:

- Asparaginase
- Caution should also be paid to the possibility of cross-resistance between clarithromycin and other macrolide drugs, as well as Lincosamycin and clindamycin.

Dosage for Mycobacterial Infections:

- Dosage of clarithromycin over long periods of time for mycobacterial infections, it is often difficult to determine the minimum effective dose.

Immunocompromised Pediatric Patients:

- Treatment of disseminated MAC infections in AIDS patients should continue at the discretion of the physician. Clarithromycin should be reduced in those with severe renal impairment.

Dosage for the eradication of H. pylori associated with peptic ulcer disease:

- CLARITEK (Clarithromycin), usually in a dose of 500mg twice daily, is given with another antibiotic and either a proton pump inhibitor or a histamine H₂-receptor antagonist, for 7 to 14 days.

Dosage in renal impairment:

- For patients with CLCR < 30mL/min, with or without coexisting hepatic impairment, the dose should be halved or the dosing interval doubled.

Adverse reactions accompanying overdosage:

- Overdosage of clarithromycin can cause gastrointestinal symptoms such as abdominal pain, vomiting, nausea, and diarrhea. Adverse reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug and supportive measures.

INTERACTIONS:

- The metabolism of other drugs by this system may be inhibited by concomitant administration of clarithromycin and may be associated with elevations in serum levels of drug classes known or suspected to be metabolized by the same CYP450 and CYP3A isozymes.

Other Drug Interactions:

- There have been post-marketed reports of torsades de pointes occurring with concurrent use of clarithromycin and quinidine or disopyramide. Serum levels of these medications should be monitored during clarithromycin therapy.

Adverse effects include hypoglycemia and thrombocytopenia. Interstitial nephritis, dizziness, insomnia, hallucinations, and confusion.

Overdosage:

- Overdosage of clarithromycin can cause gastrointestinal symptoms such as abdominal pain, vomiting, nausea, and diarrhea. Adverse reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug and supportive measures.

HOW SUPPLIED:

- CLARITEK 250mg Tablets are available in blister packs of 10’s.

- CLARITEK Drops 125mg/5mL are available in 25mL.

- CLARITEK (Clarithromycin) is usually in a dose of 500mg twice daily, is given with another antibiotic and either a proton pump inhibitor or a histamine H₂-receptor antagonist.

- This package insert is continually updated from time to time.

- Please read the contents carefully before use. This package insert is continually updated from time to time.