Klaricid Tablets

**DESCRIPTION**

Klaricid (Clarithromycin) is a macrolide antibiotic indicated for the treatment of a variety of bacterial infections. It is supplied as film coated tablets in blister strips of 2x7s in carton containing clarithromycin 500 mg (List No 3368) of the antibiotic.

**INDICATIONS**

Klaricid is indicated for the treatment of infections caused by susceptible bacteria, including:

- Upper respiratory tract infections (e.g., pharyngitis, tonsillitis, sinusitis).
- Lower respiratory tract infections (e.g., pneumonia).
- Skin and soft tissue infections (e.g., cellulitis, folliculitis).
- Otitis media.
- Gastrointestinal infections (e.g., peptic ulcer).

**CONTRAINDICATIONS**

Klaricid should not be given to patients with known hypersensitivity to clarithromycin or other macrolide antibiotics.

**WARNING**

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin, and may range in severity from mild diarrhea to fatal colitis. If diarrhea persists, patients should be evaluated for this disorder.

**ADVERSE REACTIONS**

The most common side effects of Klaricid include:

- Nausea.
- Vomiting.
- Diarrhea.

**DOSE AND ADMINISTRATION**

The usual recommended dosage of clarithromycin in adults and children 12 years of age or older, is one 250 mg tablet twice daily. The dosage may be increased to 500 mg twice daily if needed.

**PHARMACOLOGY**

Clarithromycin is a semisynthetic macrolide antibiotic that inhibits bacterial protein synthesis at the ribosomal level.

**METABOLISM**

Clarithromycin is metabolized in the liver and excreted primarily in the urine. Its half-life is approximately 1 hour in adults.

**CONTRAINDICATIONS**

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- Nausea.
- Vomiting.
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Clarithromycin is a macrolide antibiotic used to treat a variety of bacterial infections. It is primarily excreted by the liver, with a small portion metabolized in the gut by the intestinal flora.

**Contraindications**
- Patients with a history of hypersensitivity to clarithromycin or other macrolides.
- Patients with known or suspected CYP3A enzyme inhibition.
- Patients with severe hepatic impairment.
- Patients with severe acquired immunodeficiency syndrome (AIDS) and Pneumocystis jirovecii pneumonia (also known as Pneumocystis carinii pneumonia).

**Interaction Summary**
- **CYP3A inhibitors**: Clarithromycin is a substrate for CYP3A and can be affected by its inhibitors. This may lead to increased plasma levels of clarithromycin, necessitating dosage adjustment. Examples of CYP3A inhibitors include cyclosporin, ketoconazole, and ritonavir.
- **CYP3A substrates**: Clarithromycin may affect the metabolism of other CYP3A substrates. It is important to monitor patients receiving concomitant therapy for potential drug interactions.

**Specific Interactions**
- **Ritonavir**: Co-administration of ritonavir with clarithromycin can lead to increased plasma concentrations of both drugs, necessitating dosage adjustment. Ritonavir is a potent inhibitor of CYP3A and can be used as a probe substrate to assess for CYP3A inhibition.
- **Tadalafil**: Clarithromycin may increase the plasma concentration of tadalafil, leading to the risk of adverse effects. Caution is advised in patients taking both medications.
- **Estrogen-containing products**: Clarithromycin may interact with estrogen-containing products, affecting their metabolism. Women taking oral contraceptives should use alternative contraception during treatment.
- **Lithium**: Clarithromycin may affect the elimination of lithium, leading to toxic levels. Monitoring of lithium levels is recommended in patients taking both medications.

**Special Populations**
- **Pediatric patients**: Clarithromycin is not recommended for use in children under 6 months of age due to the risk of diarrhea.
- **Elderly patients**: Clarithromycin may be more prone to drug interactions in elderly patients, necessitating careful monitoring and dose adjustment.
- **Patients with renal impairment**: Clarithromycin is primarily excreted unchanged by the kidneys. Dose adjustments are necessary in patients with renal impairment to avoid toxicity.

**Pharmacokinetics**
- Clarithromycin is primarily metabolized by CYP3A4, and CYP3A inhibitors can lead to increased plasma concentrations. Clarithromycin is also a substrate for the efflux transporter, P-glycoprotein (Pgp), which can lead to decreased absorption and bioavailability.

**Important Considerations**
- Clarithromycin may cause QT prolongation and the risk of torsades de pointes. Patients with congestive heart failure, hypokalemia, or hypomagnesemia are at increased risk.
- Clarithromycin may induce the CYP3A isozyme, potentially leading to decreased levels of co-administered drugs.
- Clarithromycin is not recommended for use in patients with severe hepatic impairment.

**Dosage Adjustments**
- For patients with creatinine clearance (CrCl) of 15 to 60 mL/min, the dose of clarithromycin should be reduced by 50%.
- For patients with CrCl ≤ 15 mL/min, clarithromycin is contraindicated.

**References**

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**Additional Information**
- Clarithromycin is available in different strengths and formulations, including oral tablets, capsules, and suspension.
- It is important to follow the recommended dosage and duration of treatment to avoid treatment failure or resistance.
- Clarithromycin is generally well tolerated, but adverse effects such as gastrointestinal symptoms and respiratory tract infections are common.
- Patients should report any adverse effects to their healthcare provider to ensure prompt intervention and management.
The following table displays adverse reactions reported in clinical trials and from post-marketing experience with clarithromycin. These reactions are not necessarily causal in nature and cannot be estimated from the available data. Within each adverse event category, the reactions are listed in order of decreasing frequency. The reactions are classified as common (≥ 1/10), frequent (≥ 1/10 to < 1/100), infrequent (≥ 1/1000 to < 1/100), and very rare (≥ 1/10,000).

**ADVERSE REACTIONS**

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Common (≥ 1/10)</th>
<th>Frequent (≥ 1/10 to &lt; 1/100)</th>
<th>Infrequent (≥ 1/1000 to &lt; 1/100)</th>
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<tr>
<td><strong>Gastrointestinal</strong></td>
<td>Malaise, pyrexia, asthenia, dyspepsia, nausea, vomiting, distension, constipation, flatulence, diarrhea, rash, pruritus</td>
<td>Fever, chills, flu-like syndrome, injection site pain, injection site reactions, vasodilation</td>
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</table>
The kinetics of orally administered clarithromycin has been studied extensively in a number of animal species and adult "Intermediate Susceptibility" suggests the therapeutic effect of the drug may be equivocal or the organism would be with these procedures, a report from the laboratory of "susceptible" indicates the infecting organism is likely to respond to agar dilution method.

Inhibition zone diameters of this disc test with MIC values for clarithromycin. The MIC's are determined by the broth or quantitative methods that require measurement of zone diameters give the most precise estimates of susceptibility of mg/kg/day of clarithromycin was more effective than 50 mg/kg/day of erythromycin.

Campylobacter jejuni, Campylobacter, Borrelia burgdorferi, Propionibacterium acnes, Pasteurella multocida, Streptococci (Group C,F,G)

Clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

against most strains of the following microorganisms; however, the safety and effectiveness of clarithromycin in treating in vitro data also indicate clarithromycin has excellent activity against Legionella pneumophila, and Mycoplasma of erythromycin.

minimum inhibitory concentrations (MIC's) of clarithromycin are generally one log2 dilution more potent than the MIC's is highly potent against a wide variety of aerobic and anaerobic Gram-positive and Gram-negative organisms. The Clarity action by binding to the 50S ribosomal subunits of susceptible bacteria and

Microbiology

ATC-Code: J01FA09

The concentrations of clarithromycin and its 14-OH metabolite were higher and AUC was larger in subjects with renal impairment. Kelim and clarithromycin and its 14-OH metabolite were higher and AUC was larger in subjects with normal and decreased renal function. The plasma levels, half-life, Cmax and Cmin for both

Renal Impairment

Metabolism: Clarithromycin and its 14-OH metabolite distribute readily into body tissues and fluids. Limited data from a small number

Systemic effects of these deaminations give rise to the minor active metabolite, 14-OH clarithromycin. The major metabolic pathway is hydroxylated at the 14 position followed by deamination. The 14-epimer of the 14-OH metabolite is also a minor metabolite. Approximately 20% of the administered dose of clarithromycin is eliminated in the urine as the parent compound and its 14-OH metabolite. The remainder is eliminated in the feces as the parent compound, its 14-OH metabolite, and other unidentified minor metabolites.

Steady state plasma concentrations of clarithromycin and its 14-OH metabolite, but not 14-deaminated metabolites, were attained 24 hours after the final dose of 500 mg BID. At steady state, the systemic clearance was 162 liters/hour and was similar to the value observed in subjects with normal renal function. The renal clearance was 37 liters/hour and was reduced in proportion to the degree of renal impairment. The systemic clearance in subjects with end-stage renal disease (clearance of creatinine <20 mL/min) was 32% and 25% of the values in subjects with normal and decreased renal function, respectively.

Hepatic Impairment

Elderly Subjects

Concomitant Omeprazole Administration

A pharmacokinetic study was conducted to evaluate and compare the safety and pharmacokinetic profiles of multiple 500 mg oral doses of clarithromycin in elderly subjects (age 65 and older). When clarithromycin was administered with co-administration of omeprazole, the mean Cmax and AUC of clarithromycin increased by approximately 20%. When clarithromycin was administered as a single 250 mg dose, the mean Cmax and AUC with and without concomitant omeprazole were 2.8 mcg/mL and 15 mcg-hour/mL, respectively. The Tmax and half-life were 0.8 and 2.0 hours, respectively. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole.

A pharmacokinetic study was conducted with clarithromycin 500 mg t.i.d. and omeprazole 20 mg once daily. When the effects of omeprazole on the pharmacokinetics of clarithromycin were assessed in elderly subjects, the mean Cmax and AUC of clarithromycin increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole. The mean area under the concentration-time curve (AUC) of clarithromycin was increased by approximately 20% when concomitantly administered with omeprazole.