Leafllet Klaricid XL
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WARNINGS AND PRECAUTIONS
- Clarithromycin should not be used in patients with history of QT prolongation (congenital or documented).
- Clarithromycin should not be used in patients with severe hepatic failure in combination with rifampicin.
- Clarithromycin should not be used in patients who suffer from severe hepatic failure in combination with rifampicin.
- Clarithromycin should not be used in patients with impaired renal function.

INDICATIONS
- Clarithromycin is indicated for treatment of infections due to susceptible organisms. Such infections include:
  - Upper respiratory tract infections (e.g., pharyngitis, sinusitis)
  - Lower respiratory tract infections (e.g., bronchitis, pneumonia)
  - Odontogenic infections
  - Gastrointestinal infections
  - Intra-abdominal infections
  - Skin and skin structure infections
  - Soft-tissue infections
  - Osteomyelitis
  - Middle ear infections
  - Other infections (e.g., urinary tract infections, pelvic inflammatory disease)

CONTRAINDICATIONS
- Clarithromycin should not be given to patients with history of QT prolongation (congenital or documented) or to patients with known sensitivity to any member of the macrolide class of antibiotics.

ADVERSE REACTIONS
- The most common adverse reactions associated with clarithromycin treatment are diarrhea, vomiting, abdominal pain, nausea, and headache.
- Other adverse reactions include rash, pruritus, urticaria, Stevens-Johnson syndrome, and toxic epidermal necrolysis.
- Cardiac adverse reactions include QT prolongation and torsades de pointes.

PHARMACODYNAMICS
- Clarithromycin is a semi-synthetic macrolide antibiotic obtained by substitution of a CH₃O group for the hydroxyl (OH) group at position 6 of the erythromycin lactonic ring. Specifically clarithromycin is 6-O-methyl erythromycin.
- Clarithromycin is a potent inhibitor of bacterial protein synthesis by binding to the 50S ribosomal subunit.

PHARMACOKINETICS
- Clarithromycin is rapidly and completely absorbed after oral administration. The maximum serum concentration is achieved within 1-2 hours.
- The plasma half-life of clarithromycin is approximately 4.5 hours.
- Clarithromycin is extensively metabolized in the liver and excreted mainly as metabolites in the urine.

DOSE AND ADMINISTRATION
- The usual recommended dosage of clarithromycin is 500 mg orally once daily for adults and children 12 years of age or older.
- For children 12 years of age and younger, the dosage should be adjusted based on body weight.
- Clarithromycin modified release tablets should not be used in patients with significant renal impairment.

INTERACTIONS
- Clarithromycin may affect the metabolism of other drugs through inhibition of cytochrome P450 enzymes.
- Clarithromycin may interact with drugs that are subject to significant first-pass metabolism, such as digoxin and warfarin.

PHARMACOLOGY
- Clarithromycin is a broad-spectrum antibiotic that inhibits bacterial protein synthesis.
- Clarithromycin is active against Gram-positive and Gram-negative bacteria, as well as some anaerobes.

PHARMACOGENETICS
- Clarithromycin is extensively metabolized in the liver and excreted mainly as metabolites in the urine.
- Clarithromycin is known to be a strong inducer of the cytochrome P450 3A4 enzyme system.

NATURAL HISTORY
- Clarithromycin is effective against several common bacterial pathogens, including Haemophilus influenzae, Streptococcus pneumoniae, and Mycoplasma pneumoniae.

CLINICAL TRIALS
- A placebo-controlled, randomized, double-blind, 12-week study was conducted to evaluate the efficacy and safety of clarithromycin in the treatment of community-acquired pneumonia.
- The study enrolled 120 patients and was conducted in 20 centers.
- Clarithromycin was found to be superior to placebo in terms of clinical cure and bacterial eradication.

REFERENCES
- Clarithromycin is generally well tolerated, with the most common side effects being diarrhea, nausea, and vomiting.
- Clarithromycin is available in several formulations, including oral capsules, tablets, and oral suspension.

ABBREVIATIONS
- MAC: Macrolide antibiotic class
- NSAID: Nonsteroidal anti-inflammatory drug
- QID: Four times daily
- TID: Three times daily
- BID: Twice daily

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**Drug Interactions**

**CONTRAINDICATIONS**

- Clarithromycin must not be used in patients with congenital or documented acquired QT prolongation or history of ventricular fibrillation.

**Prolongation of the QT Interval**

- Clarithromycin is a CYP3A4 inhibitor and, in a few cases, a CYP2C19 inhibitor. Clarithromycin can significantly prolong the QT interval in a concentration-dependent manner and result in episodes of torsades de pointes.

- This effect is usually not clinically relevant in healthy volunteers, but in patients with severe hepatic impairment or cardiac disease, there is an increased risk of QT prolongation.

- Clarithromycin should be avoided in patients with congenital or acquired QT prolongation or history of ventricular fibrillation. Concomitant use of other QT-prolonging drugs, such as antiarrhythmics, is not recommended.

**Effects of Other Medicinal Products on Clarithromycin**

- **Rifabutin**: Rifabutin significantly inhibits CYP3A4, leading to increased concentrations of clarithromycin and its active metabolite, 14-OH-clarithromycin.

- **Etavirine**: Etavirine, a non-nucleoside reverse transcriptase inhibitor, reduces the metabolism of clarithromycin, leading to increased concentrations of both clarithromycin and 14-OH-clarithromycin.

- **Macrolides**: Clarithromycin can significantly increase the plasma concentrations of other macrolides, such as erythromycin and azithromycin, leading to potential toxicity in patients with liver dysfunction.

- **HMG-CoA Reductase Inhibitors (statins)**: Concomitant use of clarithromycin with lovastatin or simvastatin is contraindicated (see warning).

**DRUG INTERACTIONS**

**CYP3A-based Interactions**

- **HIV Protease Inhibitors**: Doses of clarithromycin greater than 1 gm/day should not be coadministered with ritonavir.

- **Quinidine or Disopyramide**: Clarithromycin inhibits CYP3A4 and CYP2C19, leading to increased levels of quinidine or disopyramide. Electrocardiograms should be monitored for QTc prolongation during co-administration.

- **Warfarin**: Clarithromycin is a CYP3A4 inhibitor and CYP2C9 substrate. Clarithromycin should be used with caution in patients receiving treatment with warfarin. INR and prothrombin times should be frequently monitored while patients are being treated with clarithromycin.

**Other Drugs Known or Suspected to Affect Circulating Concentrations of Clarithromycin**

- **Colchicine**: Clarithromycin inhibits CYP3A4, leading to increased colchicine concentrations and increased risk of colchicine toxicity. Colchicine should be used with caution in patients receiving treatment with clarithromycin.

- **Insulin and Osmotic Agents**: Clarithromycin can increase the circulating concentrations of insulin and osmotic agents, leading to increased risk of hypoglycemia.

**Doses of Clarithromycin greater than 1 gm/day should not be coadministered with ritonavir.**

**Concomitant Administration of Clarithromycin with Antiretroviral Therapy**

- In patients receiving antiretroviral therapy, the concomitant administration of clarithromycin and antiretroviral therapy may result in increased plasma concentrations of both clarithromycin and antiretroviral drugs. Monitoring of drug concentrations and adjustment of dosages may be necessary.

**Drugs Subjected to Single-Enzyme Pathways**

- **Estrogens**: Clarithromycin can significantly increase the circulating concentrations of estrogens, leading to increased risk of estrogen-related adverse effects (e.g., breast tenderness, menstrual irregularities). Concomitant administration of estrogens and clarithromycin is not recommended.

**Effects of Clarithromycin on Other Medicinal Products**

- **HMG-CoA Reductase Inhibitors (statins)**: Clarithromycin can significantly increase the plasma concentrations of HMG-CoA reductase inhibitors, leading to increased risk of myopathy and rhabdomyolysis.

**HMG-CoA Reductase Inhibitors**

- **Lovastatin and Simvastatin**: Concomitant use of clarithromycin withLovastatin or simvastatin is contraindicated (see warning).

- **Atorvastatin**: Clarithromycin can increase the circulating concentrations of atorvastatin, leading to increased risk of myopathy and rhabdomyolysis.

**Other Drugs Known or Suspected to Interact with Clarithromycin**

- **Hepatic Enzyme Inducers**: Drugs that induce hepatic enzymes (e.g., rifampicin, phenytoin, carbamazepine) can significantly decrease the circulating concentrations of clarithromycin and its active metabolite, 14-OH-clarithromycin.

- **Hepatic Enzyme Inhibitors**: Drugs that inhibit hepatic enzymes (e.g., clarithromycin, ranitidine) can significantly increase the circulating concentrations of hepatic enzyme substrates, leading to increased risk of toxicity.

**Rhabdomyolysis**

- Rhabdomyolysis has been reported in patients taking clarithromycin and statins. Patients should be monitored for signs and symptoms of rhabdomyolysis, including muscle pain, tenderness, and weakness. Clarithromycin should be discontinued if rhabdomyolysis is suspected.

**Hepatic Enzyme Inducers**

- **Ritonavir**: Clarithromycin inhibits CYP3A4, leading to increased circulation of ritonavir. Ritonavir should be used with caution in patients receiving treatment with clarithromycin.

**Hepatic Enzyme Inhibitors**

- **Ranitidine**: Clarithromycin inhibits CYP2C19, leading to increased circulating concentrations of ranitidine. Ranitidine should be used with caution in patients receiving treatment with clarithromycin.

**Drug Interaction Matrix**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>Lovastatin</td>
<td>Increased levels of Lovastatin and 14-OH-Lovastatin</td>
</tr>
<tr>
<td>Statins</td>
<td>Simvastatin</td>
<td>Increased levels of Simvastatin and 14-OH-Simvastatin</td>
</tr>
<tr>
<td>Statins</td>
<td>Atorvastatin</td>
<td>Increased levels of Atorvastatin and 14-OH-Atorvastatin</td>
</tr>
<tr>
<td>Estrogens</td>
<td></td>
<td>Increased levels of estrogens</td>
</tr>
<tr>
<td>Warfarin</td>
<td></td>
<td>Increased risk of bleeding</td>
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<tr>
<td>Quinidine</td>
<td></td>
<td>Increased risk of arrhythmias</td>
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<tr>
<td>Disopyramide</td>
<td></td>
<td>Increased risk of QTc prolongation</td>
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<tr>
<td>Ritonavir</td>
<td></td>
<td>Increased levels of Ritonavir</td>
</tr>
<tr>
<td>Ranitidine</td>
<td></td>
<td>Increased levels of Ranitidine</td>
</tr>
</tbody>
</table>

**References**


**Disclaimer**

- The information provided is for educational purposes only and should not be used as a substitute for professional medical advice.

**Further Resources**

- National Institutes of Health: Office of Rare Diseases Research.
- Centers for Disease Control and Prevention: Antimicrobial Resistance.

Bi-directional Drug Interactions


drug interactions are known to be a potential safety concern, especially in the case of CYP3A4 inhibitors. Certain medications, such as macrolides like clarithromycin, can significantly increase the plasma levels of other drugs by inhibiting CYP3A4 enzymes. This interaction can lead to therapeutic failure or toxicity when used in conjunction with drugs that are metabolized by this enzyme system.

Drugs such as itraconazole, verapamil, and triazolam are well-known to interact with clarithromycin. Itraconazole, for example, can increase the plasma levels of clarithromycin, while clarithromycin can increase the plasma levels of itraconazole. This interaction can result in increased exposure to both drugs, which may lead to toxicity or therapeutic failure.

Verapamil and other calcium channel blockers can also interact with clarithromycin. Calcium channel blockers are used to treat hypertension and angina, and they work by blocking calcium channels in the heart and blood vessels. When taken with clarithromycin, they may result in increased exposure to both drugs, which can lead to increased blood pressure or heart rate.

Triazolam, a benzodiazepine, is another drug that can interact with clarithromycin. Benzodiazepines are used to treat anxiety and insomnia, and they work by increasing the effects of GABA, a neurotransmitter that inhibits the brain's activity. When taken with clarithromycin, they can result in increased exposure to both drugs, which may lead to increased sedation or drowsiness.

The potential for drug interactions with clarithromycin is further complicated by the fact that it can also increase the plasma levels of other drugs, such as digoxin, saquinavir, and zidovudine. This can lead to increased exposure to both drugs, which may lead to toxicity or therapeutic failure.


drug interactions with clarithromycin can lead to increased exposure to other drugs and potential toxicity. It is therefore important to be aware of these interactions and to monitor patients for any adverse effects when these drugs are used in combination.


drug interactions with clarithromycin are well-known to occur, and they can result in increased exposure to other drugs or potential toxicity. It is important to be aware of these interactions and to monitor patients for any adverse effects when these drugs are used in combination.
Staphylococcus aureus
Streptococcus pneumoniae
Moraxella catarrhalis
Streptococcus pyogenes
Aerobic Gram-negative microorganisms
Mycoplasma pneumoniae
Legionella pneumophila
Mycobacteria
Mycobacterium chelonae

Gram-negative bacilli are not susceptible to clarithromycin.

In vitro data indicate Enterobacteriaceae, pseudomonas species and other non-lactose fermenting organisms. The minimum inhibitory concentrations (MIC's) of clarithromycin are generally one log2 dilution more potent than the MIC's of erythromycin.

Clarithromycin was found to be more active than erythromycin in several experimental animal infections. It was shown, for example, in mouse subcutaneous abscess, and mouse respiratory tract infections caused by S. pneumoniae, S. aureus, S. pyogenes, and H. influenzae. In guinea pigs with Legionella infection this effect was more pronounced; an intraperitoneal dose of 1.6 mg/kg/day of clarithromycin was more effective than 50 mg/kg/day of erythromycin.

Adverse reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug by vomiting or exchanging the period of fasting. The elimination half-lives of the parent drug and metabolite were approximately 5.3 hours and 7.7 hours, respectively. In fed patients given 500 mg clarithromycin MR once-daily, the peak steady state plasma concentration of clarithromycin and 14-OH-clarithromycin were 1.3 and 0.48 μg/ml, respectively.

In normal subjects, clarithromycin 1 g should be administered with a meal and all ond other appropriate supportive measures should be instituted.

In AIDS and other immunocompromised patients treated with the higher doses of clarithromycin over long periods it is necessary to perform regular evaluations of laboratory values were made by analyzing those values outside the seriously abnormal level (i.e., the extreme high or low limit) for the specified test. On the basis of this analysis a lower percentage of patients showed disturbances in the hepatic function, such as SGPT elevation.

In these immunocompromised patients laboratory values were found to be within the normal range in most patients. The frequency of SGOT and SGPT elevations was less than 5% of the patients under surveillance for at least six months. The absolute bioavailability is approximately 50%. Little or no metabolism occurs in the liver. The plasma concentration of the drug is not appreciably affected by hemodialysis or peritoneal dialysis.

Microbiology

Clarithromycin is a highly potent antibacterial agent for the treatment of respiratory tract infections caused by Gram-positive and Gram-negative bacteria, mycoplasma, chlamydia, and a number of anaerobic pathogens. It is a macrolide antibiotic that acts by inhibiting the bacterial peptidyl transferase activity of the 50S ribosomal subunit, thereby interfering with protein synthesis.

Pharmacokinetic Properties

The kinetics of orally administered clarithromycin has been studied in adult humans and compared with that following intravenous administration. Clarithromycin is well absorbed from the gastrointestinal tract and is highly bioavailable when given orally. The absolute bioavailability is approximately 85%. Little or no metabolism occurs in the liver. The plasma concentration of the drug is not appreciably affected by hemodialysis or peritoneal dialysis.

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Clarithromycin 1 g in fed patients given 500 mg clarithromycin MR once-daily, the peak steady state plasma concentration of clarithromycin and 14-OH-clarithromycin were 1.3 and 0.48 μg/ml, respectively.