Front

NEO-KLAR®
(Clarithromycin)

Tablets, Suspension & Drops

نیو-کلار

COMPOSITION:
NEO-KLAR Tablet 250 mg:
Each film coated tablet contains:
Clarithromycin USP ..... 250 mg.

Product Specs.: USP

NEO-KLAR Tablet 500 mg:
Each film coated tablet contains:
Clarithromycin USP ..... 500 mg.

Product Specs.: USP

NEO-KLAR Suspension 125 mg/5 ml:
Each 5 ml contains:
Clarithromycin (Granules) ..... 125 mg.

Product Specs.: USP

NEO-KLAR Suspension 250 mg/5 ml:
Each 5 ml contains:
Clarithromycin (Granules) ..... 250 mg.

Product Specs.: USP

NEO-KLAR Drops 125 mg/5 ml:
Each 5 ml contains:
Clarithromycin (Granules) ..... 125 mg.
(USP Specifications)

DESCRIPTION:
Clarithromycin is a semi-synthetic macrolide antibiotic. Chemically, it is 6-0-methylerythromycin. The molecular formula is $C_{38}H_{69}NO_{13}$, and the molecular weight is 747.96.

MECHANISM OF ACTION:
Clarithromycin exerts its antibacterial action by binding to the 50S ribosomal subunit of susceptible bacteria resulting in inhibition of protein synthesis.

PHARMACOKINETICS:
Clarithromycin is rapidly absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability of 250 mg Clarithromycin tablets was approximately 50%. For a single 500 mg dose of Clarithromycin, food slightly delays the onset of Clarithromycin absorption, increasing the peak time from approximately 2 to 2.5 hours. Food also increases the Clarithromycin peak plasma concentration by about 24%, but does not affect the extent of Clarithromycin bioavailability. Food does not affect the onset of formation of the antimicrobially active metabolite, 14-OH Clarithromycin or its peak plasma concentration but does slightly decrease the extent of metabolite formation, indicated by an 11% decrease in area under the plasma concentration-time curve (AUC). Therefore, NEO-KLAR tablets, drops or suspension may be given without regard to food. In non-fasting healthy human subjects (males and females); peak plasma concentrations were attained within 2 to 3 hours after oral dosing. Steady-state peak plasma Clarithromycin concentrations were attained within 3 days and were approximately 1 to 2 mcg/mL with a 250 mg dose administered every 12 hours and 3 to 4 mcg/mL with a 500 mg dose administered every 8 to 12 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. Clarithromycin and the 14-OH Clarithromycin metabolite distribute readily into body tissues and fluids. There are no data available on cerebrospinal fluid penetration. Because of high intracellular concentrations, tissue concentrations are higher than serum concentrations. For adult patients, the bioavailability of 10 mL of the 125 mg/5 mL suspension or 10 mL of the 250 mg/5 mL suspension is similar to a 250 mg or 500 mg tablet, respectively. In children requiring antibiotic therapy, administration of 7.5 mg/kg q12h doses of Clarithromycin as the suspension generally resulted in steady-state peak plasma concentrations of 3 to 7 mcg/mL for Clarithromycin and 1 to 2 mcg/mL for 14-OH Clarithromycin.
Special Populations:
Pediatric use: Safety and effectiveness of Clarithromycin in pediatric patients under 6 months of age have not been established.
Geriatric patients: In a steady-state study in which healthy elderly subjects (age 65 to 81 years old) were given 500 mg every 12 hours, the maximum serum concentrations and area under the curves of Clarithromycin and 14-OH Clarithromycin were increased compared to those achieved in healthy young adults. These changes in pharmacokinetics parallel known age-related decreases in renal function. In clinical trials, elderly patients did not have an increased incidence of adverse events when compared to younger patients. Dosage adjustment should be considered in elderly patients with severe renal impairment. Elderly patients may be more susceptible to development of torsades de pointes arrhythmias than younger patients.

MICROBIOLOGY:
Clarithromycin is active in vitro against a variety of aerobic and anaerobic Gram-positive and Gram-negative bacteria as well as most Mycobacterium avium complex (MAC) bacteria. Additionally, the 14-OH Clarithromycin metabolite also has clinically significant antimicrobial activity. The14-OH Clarithromycin is twice as active against Haemophilus influenzae microorganisms as the parent compound. Clarithromycin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections
Aerobic gram-positive microorganisms:
Staphylococcus aureus
Streptococcus pneumoniae
Streptococcus pyogenes
Aerobic gram-negative microorganisms:
Haemophilus influenzae
Haemophilus parainfluenzae
Moraxella catarrhalis
Other microorganisms:
Mycoplasma pneumoniae
Chlamydia pneumoniae
Mycobacteria:
Mycobacterium avium complex (MAC) consisting of:
Mycobacterium avium
Mycobacterium intracellulare
Beta-lactamase production should have no effect on Clarithromycin activity.

NOTE:
Most isolates of methicillin-resistant and oxacillin-resistant staphylococci are resistant to Clarithromycin. Omeprazole/Clarithromycin dual therapy; ranitidine bismuth citrate/Clarithromycin dual therapy; omeprazole/Clarithromycin/amoxicillin triple therapy; and lansoprazole/Clarithromycin/amoxicillin triple therapy have been shown to be active against most strains of Helicobacter pylori in vitro and in clinical infections.

INDICATIONS:
NEO-KLAR (Clarithromycin tablets, USP) and NEO-KLAR (Clarithromycin for oral suspension, USP and oral drops) are indicated for the treatment of mild to moderate infections caused by susceptible isolates of the designated bacteria in the conditions as listed below:
Adults:
Pharyngitis/Tonsillitis due to Streptococcus pyogenes (The usual drug of choice in the treatment and prevention of streptococcal infections and the prophylaxis of rheumatic fever is penicillin administered by either the intramuscular or the oral route. Clarithromycin is generally effective in the eradication of S. pyogenes from the nasopharynx; however, data establishing the efficacy of Clarithromycin in the subsequent prevention of rheumatic fever are not available at present). Acute maxillary sinusitis due to Haemophilus influenzae, Moraxella catarrhalis or Streptococcus pneumoniae. Acute bacterial exacerbation of chronic bronchitis due to Haemophilus influenzae, Haemophilus parainfluenzae, Moraxella catarrhalis, or Streptococcus pneumoniae. Community-Acquired pneumoniae due to Haemophilus influenzae, Mycoplasma pneumoniae, Streptococcus pneumoniae, or Chlamydia pneumoniae. Uncomplicated skin and skin structure infections due to Staphylococcus aureus, or Streptococcus pyogenes (Abscesses usually require surgical drainage). Disseminated mycobacterial infections due to Mycobacterium avium, or Mycobacterium intracellulare NEO-KLAR (Clarithromycin) tablets in combination with amoxicillin and lansoprazole or omeprazole, as triple therapy, are indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or five-year history of duodenal ulcer) to eradicate H. pylori. NEO-KLAR tablets in combination with omeprazole capsules or ranitidine bismuth citrate tablets are also indicated for the treatment of patients with an active duodenal ulcer associated with H. pylori infection. However, regimens which contain Clarithromycin as the single antimicrobial agent are more likely to be associated with the development of Clarithromycin resistance among patients who fail therapy. Clarithromycin-containing regimens should not be used in patients with known or suspected Clarithromycin resistant isolates because the efficacy of treatment is reduced in this setting. In patients who fail therapy, susceptibility testing should be done if possible. If resistance to Clarithromycin is demonstrated, a non-Clarithromycin-containing therapy is recommended.
Children (6months-12 years) (NEO-KLAR oral suspension/oral drops):
Pharyngitis/Tonsillitis due to Streptococcus pyogenes.
Community-Acquired pneumoniae due to Mycoplasma pneumoniae, Streptococcus pneumoniae, or Chlamydia pneumoniae (TWAR)
Acute maxillary sinusitis due to Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae
Acute otitis media due to Haemophilus influenzae, Moraxella catarrhalis, or Streptococcus pneumoniae.

DOSAGE & ADMINSTRATION:
NEO-KLAR (Clarithromycin tablets, USP) and NEO-KLAR (Clarithromycin for oral suspension or oral drops, USP) may be given with or without food.
Adults: The adult dosage of NEO-KLAR for respiratory tract infections is 250 mg to 500 mg every 12 hours for 7 to 14 days. For infections caused by less susceptible organisms, the upper dosage should be used.

Dosage Guidelines for NEO-KLAR Tablets:

Infection	Dosage BD	Duration
Pharyngitis/tonsillitis	250 mg	10 days
Acute maxillary sinusitis	500 mg	7-14 days
Acute exacerbation of chronic bronchitis and pneumoniae	250-500 mg	7-14 days
Uncomplicated Skin and Skin Structure Infection	250-500 mg	7-14 days

In the treatment of Group A streptococcus infections, therapy should be continued for 10 days.
Renal impairment: In patients with renal impairment and a creatinine clearance < 30 mL/min., the dosage of NEO-KLAR should be reduced by one-half, i.e., 250 mg once daily, or 250 mg twice daily in more severe infections. Dosage should not be continued beyond 14 days in these patients. The safety and efficacy of 500 mg Clarithromycin in patients with severe renal impairment has not been established.
Hepatic impairment: In patients with a combination of hepatic (mild to moderate) and renal impairments, decreased dosage of Clarithromycin or prolonged dosing intervals may be appropriate. Clarithromycin may be administered without dosage adjustment in the presence of hepatic impairment if there is normal renal function. Clarithromycin is contraindicated in patients with severe hepatic failure in combination with renal impairment.
Eradication of helicobacter pylori:
Triple therapy:
NEO-KLAR/omeprazole/amoxicillin: The recommended dose is Clarithromycin 500 mg twice daily in conjunction with omeprazole 20 mg daily and amoxicillin 1000 mg twice daily for 10 days.
Adults with mycobacterial infections:
Prophylaxis: The recommended dose of NEO-KLAR for the prevention of disseminated M. avium disease is 500 mg twice daily.
Treatment: Clarithromycin is recommended as the primary agent for the treatment of disseminated infection due to MAC. The recommended dose for mycobacterial infections in adults is 500 mg twice daily.
NEO-KLAR oral suspension:
Adults: The recommended daily dosage of NEO-KLAR (Clarithromycin for oral suspension USP) is 15 mg/kg/day, in divided doses every 12 hours, not to exceed 1000 mg/day. The usual duration of treatment is for 5 to 10 days depending on the pathogen involved and the severity of the condition. Treatment for pharyngitis caused by Streptococcal species should be 10 days.
Children: In children with renal impairment and a creatinine clearance < 30 mL/min, the dosage of NEO-KLAR should be reduced by one-half, i.e., up to 250 mg once daily, or 250 mg twice daily in more severe infections. Dosage should not be continued beyond 14 days in these patients.
Pediatric dosage guidelines:
Based on body weight:

WEIGHT	125 MG/ 5ML DOSAGE (ml) given twice a day
8 to 11 kg (1 to 2 years)	**2.5**
12 to 19 kg (2 to 4 years)	5
20 to 29 kg (4 to 8 years)	7.5
30 to 40 kg (8 to 12 years)	10

Children < 8 kg should be dosed on a per kg basis (approximately 7.5 mg/kg twice daily).

Children with mycobacterial infections:
In children, the recommended dose is 7.5 mg/kg twice daily up to 500 mg twice daily Clarithromycin per day in 2 divided doses.

CONTRAINDICATIONS:
Clarithromycin is contraindicated in patients with a known hypersensitivity to Clarithromycin, erythromycin, or any of the macrolide antibiotics. Clarithromycin is contraindicated in patients with a history of cholestatic jaundice/hepatic dysfunction associated with prior use of Clarithromycin. Concomitant administration of Clarithromycin and any of the following drugs is contraindicated: cisapride, pimozide, astemizole, terfenadine, and ergotamine or dihydroergotamine. There have been post-marketing reports of drug interactions when Clarithromycin and/or erythromycin are co-administered with cisapride, pimozide, astemizole, or terfenadine resulting in cardiac arrhythmias (QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsades de pointes) most likely due to inhibition of metabolism of these drugs by erythromycin and Clarithromycin. Fatalities have been reported. Concomitant administration of Clarithromycin and colchicine is contraindicated in patients with renal or hepatic impairment. Contraindicated in patients with history of QT prolongation or ventricular cardiac arrhythmia, including torsades de pointes. Also contraindicated in patients with hypokalaemia due to the risk of prolongation of QT-time and torsades de pointes.
Concomitant therapy with HMG-CoA reductase inhibitors (statins) that are extensively metabolized by CYP3A4 (lovastatin or simvastatin), due to an increased risk of myopathy, including rhabdomyolysis.
Concomitant therapy with ergot alkaloids (e.g., ergotamine or dihydroergotamine) as this may result in ergot toxicity. Concomitant administration with oral midazolam, ticagrelor or ranolazine Concomitant therapy with colchicine due to the risk of life threatening and fatal colchicine toxicity. This risk may be further increased with concomitant medications metabolized by P-glycoprotein or strong CYP3A inhibitors.

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WARNINGS:

Use in pregnancy:

Clarithromycin should not be used in pregnant women except in clinical circumstances where no alternative therapy is appropriate. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus. Clarithromycin has demonstrated adverse effects of pregnancy outcome and/or embryo-fetal development in monkeys, rats, mice, and rabbits at doses that produced plasma levels 2 to 17 times the serum levels achieved in humans treated at the maximum recommended human doses.

Hepatotoxicity:

Hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice, has been reported with Clarithromycin. This hepatic dysfunction may be severe and is usually reversible. In some instances, hepatic failure with fatal outcome has been reported and generally has been associated with serious underlying diseases and/or concomitant medications. Discontinue Clarithromycin immediately if signs and symptoms of hepatitis occur.

QT Prolongation:

Clarithromycin has been associated with prolongation of the QT interval and infrequent cases of arrhythmia. Cases of torsades de pointes have been spontaneously reported during postmarketing surveillance in patients receiving Clarithromycin. Fatalities have been reported. Clarithromycin should be avoided in patients with ongoing proarrhythmic conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia and in patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval.

DRUG INTERACTIONS:

Serious adverse reactions have been reported in patients taking Clarithromycin concomitantly with CYP3A4 substrates. These include colchicine toxicity with colchicine; rhabdomyolysis with simvastatin, lovastatin, and atorvastatin; and hypotension with calcium channel blockers metabolized by CYP3A4 (e.g., verapamil, amlodipine, diltiazem). Life-threatening and fatal drug interactions have been reported in patients treated with Clarithromycin and colchicine. Clarithromycin is a strong CYP3A4 inhibitor and this interaction may occur while using both drugs at their recommended doses. If co-administration of Clarithromycin and colchicine is necessary in patients with normal renal and hepatic function, the dose of colchicine should be reduced. Patients should be monitored for clinical symptoms of colchicine toxicity. Concomitant administration of Clarithromycin and colchicine is contraindicated in patients with renal or hepatic impairment.

Clostridium difficile associated diarrhea:

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including NEO-KLAR, and may range in severity from mild diarrhea to fatal colitis. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

PRECAUTIONS:

Prescribing NEO-KLAR in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Clarithromycin is principally excreted via the liver and kidney. Clarithromycin may be administered without dosage adjustment to patients with hepatic impairment and normal renal function. However, in the presence of severe renal impairment with or without coexisting hepatic impairment, decreased dosage or prolonged dosing intervals may be appropriate.
Clarithromycin in combination with ranitidine bismuth citrate therapy is not recommended in patients with creatinine clearance less than 25 mL/min.
Clarithromycin in combination with ranitidine bismuth citrate should not be used in patients with a history of acute porphyria.
Exacerbation of symptoms of myasthenia gravis and new onset of symptoms of myasthenic syndrome has been reported in patients receiving Clarithromycin therapy.

PREGNANCY & LACTATION

Pregnancy: Pregnancy Category C. Clarithromycin should not be used in pregnancy except where no alternative therapy is appropriate, particularly during the first 3 months of pregnancy. If pregnancy occurs while taking the drug, the patient should be apprised of the potential hazard to the fetus. Nursing Mothers: Clarithromycin is excreted in human milk. Caution should be exercised when Clarithromycin is administered to a nursing woman.

DRUG INTERACTIONS:

Clarithromycin use in patients who are receiving theophylline may be associated with an increase of serum theophylline concentrations. Monitoring of serum theophylline concentrations should be considered for patients receiving high doses of theophylline or with baseline concentrations in the upper therapeutic range. Hypotension, bradyarrhythmias, and lactic acidosis have been observed in patients receiving concurrent verapamil, belonging to the calcium channel blockers drug class. Concomitant administration of single doses of Clarithromycin and carbamazepine has been shown to result in increased plasma concentrations of carbamazepine. Blood level monitoring of carbamazepine may be considered. When Clarithromycin and terfenadine were coadministered, plasma concentrations of the active acid metabolite of terfenadine were threefold higher, on average, than the values observed when terfenadine was administered alone. The pharmacokinetics of Clarithromycin and the 14-OH-Clarithromycin were not significantly affected by co-administration of terfenadine once Clarithromycin reached steady-state conditions. Concomitant administration of Clarithromycin with terfenadine is contraindicated. Simultaneous oral administration of NEO-KLAR tablets and zidovudine to HIV-infected adult patients may result in decreased steady-state zidovudine concentrations. Clarithromycin may be administered without dosage adjustment to patients with normal renal function taking ritonavir. Since concentrations of 14-OH Clarithromycin are significantly reduced when Clarithromycin is co-administered with ritonavir, alternative antibacterial therapy should be considered for indications other than infections due to Mycobacterium avium complex. Doses of Clarithromycin greater than 1000 mg per day should not be co-administered with protease inhibitors. Increased serum concentrations of carbamazepine and the active acid metabolite of terfenadine were observed in clinical trials with Clarithromycin.
Colchicine is a substrate for both CYP3A and the efflux transporter, P-glycoprotein (Pgp). Clarithromycin and other macrolides are known to inhibit CYP3A and Pgp. The dose of colchicine should be reduced when co-administered with Clarithromycin in patients with normal renal and hepatic function. Concomitant use of Clarithromycin and colchicine is contraindicated in patients with renal or hepatic impairment. Inducers of CYP3A enzymes, such as efavirenz, nevirapine, rifampicin, rifabutin, and rifapentine will increase the metabolism of Clarithromycin, thus decreasing plasma concentrations of Clarithromycin, while increasing those of 14-OH-Clarithromycin. Since the microbiological activities of Clarithromycin and 14-OH Clarithromycin are different for different bacteria, the intended therapeutic effect could be impaired during concomitant administration of Clarithromycin and enzyme inducers. Alternative antibacterial treatment should be considered when treating patients receiving inducers of CYP3A. Phosphodiesterase inhibitors are primarily metabolized by CYP3A, and CYP3A will be inhibited by concomitant administration of Clarithromycin. Co-administration of Clarithromycin with sildenafil, tadalafil, or vardenafil will result in increased exposure of these phosphodiesterase inhibitors. Co -administration of these phosphodiesterase inhibitors with Clarithromycin is not recommended. The primary route of metabolism for tolterodine is via CYP2D6. However, in a subset of the population devoid of CYP2D6, the identified pathway of metabolism is via CYP3A. In this population subset, inhibition of CYP3A results in significantly higher serum concentrations of tolterodine. Tolterodine 1 mg twice daily is recommended in patients deficient in CYP2D6 activity (poor metabolizers) when co-administered with Clarithromycin. Triazolobenzodiazepines (e.g., alprazolam, midazolam, triazolam): When oral midazolam is co-administered with Clarithromycin, dose adjustments may be necessary and possible prolongation and intensity of effect should be anticipated. Caution and appropriate dose adjustments should be considered when triazolam or alprazolam is co-administered with Clarithromycin. For benzodiazepines which are not metabolized by CYP3A (e.g., temazepam, nitrazepam, lorazepam), a clinically important interaction with Clarithromycin is unlikely. Monitoring the patient for increased CNS pharmacological effects is suggested. Both Clarithromycin and atazanavir are substrates and inhibitors of CYP3A, and there is evidence of a bi directional drug interaction. When Clarithromycin is co-administered with atazanavir, the dose of Clarithromycin should be decreased by 50%. Since concentrations of 14-OH Clarithromycin are significantly reduced when Clarithromycin is co-administered with atazanavir, alternative antibacterial therapy should be considered for indications other than infections due to Mycobacterium avium complex . Doses of Clarithromycin greater than 1000 mg per day should not be co-administered with protease inhibitors. Both Clarithromycin and itraconazole are substrates and inhibitors of CYP3A, potentially leading to a bi directional drug interaction when administered concomitantly. Clarithromycin may increase the plasma concentrations of itraconazole, while itraconazole may increase the plasma concentrations of Clarithromycin. Patients taking itraconazole and Clarithromycin concomitantly should be monitored closely for signs or symptoms of increased or prolonged adverse reactions. Both Clarithromycin and saquinavir are substrates and inhibitors of CYP3A and there is evidence of a bi directional drug interaction. No dose adjustment of Clarithromycin is necessary when Clarithromycin is co-administered with saquinavir in patients with normal renal function. When saquinavir is co-administered with ritonavir, consideration should be given to the potential effects of ritonavir on Clarithromycin.

The following CYP3A based drug interactions have been observed with erythromycin products and/or with Clarithromycin in post-marketing experience:

There have been reports of torsades de pointes occurring with concurrent use of Clarithromycin and quinidine or disopyramide. Electrocardiograms should be monitored for QTc prolongation during co-administration of Clarithromycin with these drugs. Serum concentrations of these medications should also be monitored. Co-administration of Clarithromycin with ergotamine or dihydroergotamine has been associated with acute ergot toxicity characterized by vasospasm and ischemia of the extremities and other tissues including the central nervous system. Concomitant administration of Clarithromycin with ergotamine or dihydroergotamine is contraindicated. As with other macrolides, Clarithromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g., atorvastatin, lovastatin and simvastatin). Rarely of rhabdomyolysis may occur in patients taking these drugs concomitantly.

ADVERSE EFFECTS:

The most frequent adverse events in adults taking Clarithromycin are diarrhea, nausea, abnormal taste, dyspepsia, abdominal pain/discomfort, and headache. In pediatric patients, the most frequently adverse events are diarrhea, vomiting, abdominal pain, rash, and headache. Most of these events are mild or moderate in severity. Allergic reactions ranging from urticaria and mild skin eruptions to rare cases of anaphylaxis, Stevens-Johnson syndrome and toxic epidermal necrolysis have occurred. Other adverse events include glossitis, stomatitis, oral moniliasis, anorexia, vomiting, pancreatitis, tongue discoloration, thrombocytopenia, leukopenia, neutropenia, and dizziness. There have been rare cases of tooth discoloration in patients treated with Clarithromycin. Tooth discoloration is usually reversible with professional dental cleaning.There have been isolated reports of hearing loss, which is usually reversible, occurring chiefly in elderly women. Reports of alterations of the sense of smell including smell loss, usually in conjunction with taste perversion or taste loss have also been reported. Transient CNS events including anxiety, behavioral changes, confusional states, convulsions, depersonalization, disorientation, hallucinations, insomnia, depression, manic behavior, nightmares, psychosis, tinnitus, tremor, and vertigo have been reported. Events usually resolve with discontinuation of the drug. Adverse reactions related to hepatic dysfunction may also occur. There have been rare reports of hypoglycemia, some of which have occurred in patients taking oral hypoglycemic agents or insulin. As with other macrolides, Clarithromycin has been associated with QT prolongation and ventricular arrhythmias, including ventricular tachycardia and torsades de pointes. There have been rare cases of interstitial nephritis coincident with Clarithromycin use. There have been cases of colchicine toxicity with concomitant use of Clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency. Deaths have been reported in some such patients.

Changes in laboratory values:

Changes in laboratory values with possible clinical significance were as follows:
Hepatic: Elevated SGPT (ALT), SGOT (AST), GGT; alkaline phosphatase; LDH; total bilirubin.
Hematologic: Decreased WBC; elevated prothrombin time
Renal: Elevated BUN; elevated serum creatinine

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. As with other macrolides, Clarithromycin serum concentrations are not expected to be appreciably affected by hemodialysis or peritoneal dialysis.

RECONSTITUTION:

For Suspension 125 mg/5 ml:
Add freshly boiled and cooled water in bottle and shake well to make 60 ml up to the red mark on the bottle.
For Suspension 250 mg/5 ml:
Add freshly boiled and cooled water in bottle and shake well to make 70 ml up to the red mark on the bottle.
DOSAGE:
For children 7.5 mg / kg after every 12 hour or as directed by the physician.
For Drops 125 mg / 5 ml:
Add freshly boiled and cooled water in bottle and shake well to make 30 ml up to the red mark on the bottle.
DOSAGE:
For children 7.5 mg / kg after every 12 hours. For accurate measurement of dosage a dropper of 2.5 ml is provided or as directed by the physician.

INSTRUCTIONS:

For Tablet:
Store below 30ºC. Protect from heat, sunlight and moisture. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.
For Suspension:
Store below 30ºC. Store at cool dry place and protect from sunlight. Shake well before use. Keep bottle tightly closed after use. Use within 14 days after reconstitution. Keep out of the reach of children.
Do not refrigerate reconstituted suspension. To be sold on the prescription of a registered medical practitioner only.
For Drops:
Store below 30ºC. Store at cool dry place and protect from sunlight. Shake well before use. Keep bottle tightly closed after use. Use within 14 days after reconstitution. Keep out of the reach of children.
Do not refrigerate reconstituted suspension. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

NEO-KLAR Tablet 250 mg	:	Pack of 1x10 tablets.
NEO-KLAR Tablet 500 mg	:	Pack of 1x10 tablets.
NEO-KLAR Suspension 125 mg/5 ml	:	Bottle of 60 ml.
NEO-KLAR Suspension 250 mg/5 ml	:	Bottle of 70 ml.
NEO-KLAR Drops 125 mg/5 ml	:	Bottle of 30 ml.

ہدایات برائے ٹیبلٹس
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

بنانے کا طریقہ:

سسپنشن برائے ***125 mg/5 ml*** :

تازہ اُبلا ہوا ٹھنڈا پانی بھر کر بوتل میں ڈالیں اور اچھی طرح ہلا لیں تا کہ
بوتل پر دیئے گئے سرخ نشان تک ۶۰ ملی لیٹر سسپنشن تیار ہو جائے۔

سسپنشن برائے ***250 mg/5 ml*** :

تازہ اُبلا ہوا ٹھنڈا پانی بھر کر بوتل میں ڈالیں اور اچھی طرح ہلا لیں تا کہ
بوتل پر دیئے گئے سرخ نشان تک ۷۰ ملی لیٹر سسپنشن تیار ہو جائے۔

خوراک:

بچوں کیلئے ۷.۵ ملی گرام فی کلوگرام ہر ۱۲ گھنٹے کے بعد یا ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ خشک اور ٹھنڈی جگہ پر
روشنی سے محفوظ رکھیں۔ استعمال سے قبل بوتل کو اچھی طرح ہلا لیں۔
استعمال کے بعد بوتل کو اچھی طرح بند کر کے رکھیں۔ سسپنشن بنانے کے
بعد ۱۴ دن کے اندر استعمال کریں۔ بچوں کی پہنچ سے دور رکھیں۔
تیار شدہ دوا ریفریجریٹر میں نہ رکھیں ۔ صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

بنانے کا طریقہ:

ڈراپس برائے ***125 mg/5 ml*** :

تازہ اُبلا ہوا ٹھنڈا پانی بھر کر بوتل میں ڈالیں اور اچھی طرح ہلا لیں تا کہ
بوتل پر دیئے گئے سرخ نشان تک ۶۰ ملی لیٹر سسپنشن تیار ہو جائے۔

خوراک:

بچوں کیلئے ۷.۵ ملی گرام فی کلوگرام ہر ۱۲ گھنٹے کے بعد استعمال کریں۔
خوراک کی صحیح پیمائش کیلئے ۲.۵ ملی لیٹر ڈراپر ہمراہ ہے یا ڈاکٹر کی ہدایت
کے مطابق استعمال کریں۔

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ خشک اور ٹھنڈی جگہ پر
روشنی سے محفوظ رکھیں۔ استعمال سے قبل بوتل کو اچھی طرح ہلا لیں۔
استعمال کے بعد بوتل کو اچھی طرح بند کر کے رکھیں۔ سسپنشن بنانے کے
بعد ۱۴ دن کے اندر استعمال کریں۔ بچوں کی پہنچ سے دور رکھیں۔
تیار شدہ دوا ریفریجریٹر میں نہ رکھیں۔ صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT.

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