Biotransformation
The microbiologically active metabolite 14-hydroxyclarithromycin is formed by first pass metabolism as indicated by lower bioavailability of the metabolite following IV administration. Following IV administration, the blood levels of clarithromycin achieved are well in excess of the MIC 90s for the common pathogens and the levels of 14-hydroxyclarithromycin exceed the necessary concentrations for important pathogens, e.g. H. influenzae.

Excretion
The microbiologically active metabolite 14-hydroxyclarithromycin is excreted in the urine at 24 Hours

Storage :Store below 25°C. till reconstitution. Protect from light & moisture.
Improper storage may deteriorate the product.

MEDICINE : Keep out of reach of children.

Reconstituted solution
Chemical and physical in-use stability has been demonstrated for 24 hours at 5 - 25ºC when reconstituted in 10ml water for injections IP and for 6 hours(at 25 ºC) or 24 hours at (5 ° C) once diluted in 250ml of appropriate diluent.

Chemical and physical in-use stability would normally not be longer than 24 hours at 2 to 8°C unless reconstitution/ dilution has taken place in controlled and validated aseptic conditions.

DOSAGE FORM
Parenteral (Powder for solution for IV Infusion only.)

SHELF LIFE
Please see manufacturing date and Expiry date printed on pack. Do not use the product after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

PRESENTATION: A white dry powder filled in glass vial.

Manufactured by:
AMERICAN REMEDIES
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)

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WHO GMP CERTIFIED

OVERDOSE
In the case of over dosage, clarithromycin I.V. should be discontinued and all other appropriate supportive measures should be instituted.
Ingestion of large amounts of clarithromycin can be expected to produce gastrointestinal symptoms. Adverse reactions accompanying over dosage should be treated by the prompt elimination of unabsorbed drug and supportive measures. As with other macrolides, clarithromycin serum levels are not expected to be appreciably affected by hemodialysis or peritoneal dialysis.

INDICATIONS
- Chest infections such as bronchitis and pneumonia
- Throat and sinus infections
- Skin and soft tissue infections

DOSAGE AND ADMINISTRATION
Recommended Dosage
The recommended dosage of clarithromycin I.V. is 1.0 g daily, divided into two equal doses, each infused after further dilution with an appropriate I.V. diluent, over a 60-minute time period. At the present time, there are no data supporting intravenous use of clarithromycin in children. Clarithromycin should not be given as a bolus or an intramuscular injection.
Dosage in Patients with Mycobacterial Infections
Although, currently there is no data regarding use of clarithromycin I.V. in immunocompromised patients, data are available regarding the use of oral clarithromycin in HIV-infected patients. In disseminated or localized infections (*M. avium, M. intracellulare, M. chelonae, M. fortuitum, M. kansasii*), the recommended treatment, in adults, is 1000 mg/day in two divided doses. Intravenous therapy may be limited for up to two to five days in the very ill patient and should be changed to oral therapy whenever possible as determined by the physician.
In patients with renal impairment who have creatinine clearance less than 30 mL/min, the dosage of clarithromycin should be reduced to one half of the normal recommended dose.

Administration and Preparation Instructions
Add Not less than 10 ml Sterile Water For Injection & Shake vigorously for 5-10 minutes to obtain clear colourless solution.This provides a 5% initial solution (50mg/ml). Add above reconstituted solution to 250 ml of 5% dextrose, or 0.9% sodium chloride or lactated Ringer's Solution. Final solution to be administered has the concentration about 1.9 mg/ml.
Clarithromycin should be administered into one of the larger proximal veins as an IV infusion over 60 minutes, using a final solution (to be administered) having the concentration about 2mg/ml. Solution strengths greater than 2mg/ml must not be used. Clarithromycin should not be given as a bolus or an intramuscular injection.

USE IN SPECIAL POPULATION
Pregnancy
Pregnancy Category C
The safety of clarithromycin during pregnancy and breast feeding of infants has not been established. Clarithromycin should thus not be used during pregnancy or lactation unless the benefit is considered to outweigh the risk.

Nursing Mothers
Some animal studies have suggested an embryotoxic effect but only at dose levels which are clearly toxic to mothers. Clarithromycin has been found in the milk of lactating animals and in human breast milk.

Paediatric Use
At the present time, there are no data supporting intravenous use of clarithromycin in children.

Geriatric Use
The recommended dose for geriatric patient is as that of the adults.

Gender
No gender-related difference in the safety profile of clarithromycin is reported.

Ability to drive and operate machines
Clarithromycin may produce vertigo, dizziness, disorientation and confusion. If any of the mentioned symptoms is experienced then driving and machine operating must be avoided.

CONTRAINDICATIONS
Clarithromycin IV is contraindicated in patients with known hypersensitivity to macrolide antibiotic drugs. Allergic or hypersensitive reactions should be managed by prompt supportive measures.
Concomitant administration of clarithromycin and any of the following drugs is contraindicated: astemizole, cisapride, pimozide, terfenadine, ergotamine, dihydroergotamine, lovastatin or simvastatin

210mm

Distribution
Clarithromycin is extensively distributed in body tissues and fluids. Relevant to the treatment of respiratory tract infections, clarithromycin concentrations in tonsil and whole lung tissue are two- to six-fold higher than those observed in the serum. Mean clarithromycin concentrations in epithelial lining fluid range from 15.1 to 72.1µg/mL and mean levels in alveolar macrophages range from 818 to 1996µg/mL during the first 12 h after the completion of 500 mg q12h dosing for a total of seven or nine doses. These clarithromycin concentrations in lung epithelial lining fluid and alveolar macrophages exceeded plasma concentrations by 10- and 100-fold, respectively.

WARNINGS AND PRECAUTIONS
Caution should be exercised in administering the antibiotic to patients with impaired hepatic function. Since it is principally excreted by the liver. Caution should also be exercised when administering clarithromycin to patients with moderate to severe renal failure.
Exacerbation of symptoms of myasthenia gravis has been reported in patients receiving clarithromycin therapy.
Should not be used in pregnant women without carefully weighing the benefits against risk, particularly during the first three months of pregnancy.
Prolonged or repeated use of clarithromycin may result in an overgrowth of non-susceptible bacteria or fungi. If super-infection occurs, clarithromycin should be discontinued.
The concomitant use of clarithromycin and oral hypoglycemic agents and/or insulin can result in significant hypoglycemia. With certain hypoglycemic drugs such as nateglinide, pioglitazone, repaglinide and rosiglitazone, inhibition of CYP3A enzyme by clarithromycin may be involved and could cause hypoglycemia when used concomitantly. Careful monitoring of glucose is recommended.
There is a risk of serious hemorrhage and significant elevations in INR and prothrombin time when clarithromycin is co-administered with warfarin. INR and prothrombin times should be frequently monitored while patients are receiving clarithromycin and oral anticoagulants concurrently.
Concomitant use of clarithromycin with lovastatin or simvastatin is contraindicated. As with other macrolides, clarithromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors. Rare reports of rhabdomyolysis have been reported in patients taking these drugs concomitantly. Patients should be monitored for signs and symptoms of myopathy.

DRUG INTERACTIONS
Clarithromycin has been shown not to interact with oral contraceptives.
As with other macrolide antibiotics the use of clarithromycin in patients concurrently taking drugs metabolised by the cytochrome P450 system (e.g. warfarin, ergot alkaloids, triazolam, midazolam, disopyramide, lovastatin, rifabutin, phenytoin, cyclosporin and tacrolimus) may be associated with elevations in serum levels of these other drugs. Rhabdomyolysis, coincident with the co-administration of clarithromycin, and HMG-CoA reductase inhibitors, such as lovastatin and simvastatin has been reported.
The administration of clarithromycin to patients who are receiving theophylline has been associated with increased serum theophylline levels and potential theophylline toxicity.
The use of clarithromycin in patients receiving warfarin may result in a potentiation of the effects of warfarin. Prothrombin time should be frequently monitored in these patients.
The effects of digoxin may be potentiated with concomitant administration of clarithromycin. Monitoring of serum digoxin levels should be considered.
Clarithromycin may potentiate the effects of carbamazepine due to a reduction in the rate of excretion.
Simultaneous oral administration of clarithromycin tablets and zidovudine to HIV infected adults may result in decreased steady-state zidovudine concentrations. Since this interaction in adults is thought to be due to interference of clarithromycin with simultaneously administered oral zidovudine, this interaction should not be a problem when clarithromycin is administered intravenously. With oral clarithromycin, the interaction can be largely avoided by staggering the doses.
Ritonavir increases the area under the curve (AUC), Cmax and Cmin of clarithromycin when administered concurrently. Because of the large therapeutic window for clarithromycin, no dosage reduction should be necessary in patients with normal renal function. However, for patients with renal impairment, the following dosage adjustments should be considered: For patients with CLCR 30 to 60ml/min the dose of clarithromycin should be decreased by 50%. For patients with CLCR <30ml/min the dose of clarithromycin should be decreased by 75%. Doses of clarithromycin greater than 1g/day should not be co-administered with ritonavir.

UNDESIRABLE EFFECTS
The most frequently reported infusion-related adverse events in clinical studies were injection site inflammation, tenderness, phlebitis and pain. The most common non-infusion related adverse event reported was taste perversion.
Common adverse events: Headache, taste perversion, diarrhoea, nausea, abdominal pain, dyspepsia, vomiting, hepatic enzyme increased.
Other adverse reactions are: Anaphylactic reaction, hypersensitivity, Leucopenia, thrombocytopenia, Oral candidiasis, Psychotic disorder, hallucination, disorientation, confusional state, depersonalization, depression, anxiety, insomnia, abnormal dreams, Convulsion, dizziness, ageusia, anosmia, dysgeusia, parosmia, deafness, vertigo, tinnitus, electrocardiogram QT prolonged, ventricular tachycardia, Hepatic failure, hepatitis, hepatitis cholestatic, jaundice cholestatic, jaundice hepatocellular, hepatic function abnormal, Myalgia, rhabdomyolysis.

Only for the use of a Registered Medicinal Practitioner or a Hospital or a Laboratory.

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Clarithromycin For Infusion B.P.

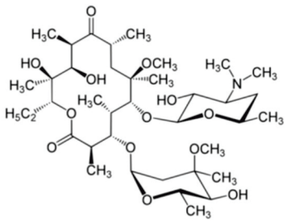
AMERICAN
CLARICAN

FOR IV INFUSION USE ONLY

Composition :
Each vial contains :

Clarithromycin (Sterile) Lyophilized	I.P.	500 mg
Lactobionic Acid		q.s.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTY
DESCRIPTION:
Clarithromycin is (3R, 4S, 5S, 6R, 7R, 9R, 11R, 12R, 13S, 14R)-4-[(2,6-dicleoxy-3-C-methyl-3-0-methyl-x-L-nbo-hexopyranosyl)oxy]-14-ethyl-12, 13-dihydroxy-7-methoxy-3, 5,7,9,11,13-hexamethyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hxopyranosyl] oxy] oxacyclotetradecane-2, 10-dione(6-0-methylerythromycin A). Its empirical formula is $C_{38}H_{69}NO_{13}$, with a molecular weight of 748 The structural formula is:



PHARMACOLOGY:
Pharmacodynamics
Mechanism of Action
Clarithromycin is a semi-synthetic derivative of erythromycin A. It exerts its antibacterial action by binding to the 50s ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis. Clarithromycin demonstrates excellent *in vitro* activity against standard strains of clinical isolates. It is highly potent against a wide variety of aerobic and anaerobic gram positive and negative organisms. The minimum inhibitory concentrations (MICs) of clarithromycin are generally two-fold lower than the MICs of erythromycin.

Microbiology:
Clarithromycin has been shown to be active against most strains of the following microorganisms.

Aerobic Gram-Positive microorganisms: *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes, Listeria monocytogenes*

Aerobic Gram-negative microorganisms: *Haemophilus influenza, Haemophilus parainfluenzae, Moraxella catarrhalis, Neisseria gonorrhoeae, Legionella pneumophila*

Other microorganisms
Mycoplasma pneumonia, Chlamydia pneumonia

Mycobacteria
Mycobacterium leprae, Mycobacterium kansasii, Mycobacterium chelonae, Mycobacterium fortuitum, Mycobacterium avium complex (MAC) consisting of: Mycobacterium avium, Mycobacterium Intracellulare

Clarithromycin has bactericidal activity against several bacterial strains. These organisms include H. influenzae, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Morazella (Brahamella) catarrhalis, Neisseria gonorrhoeae, Helicobacter pylori and Campylobacter spp. The activity of clarithromycin against H. pylori is greater at neutral pH than at acid pH.

Resistance
Most strains of methicillin-resistant and oxacillin-resistant staphylococci are resistant to clarithromycin.

Pharmacokinetics
Absorption
Clarithromycin for Infusion 500 mg is IV, 100% absorption is desired.