120 mm

210 mm

Rithmo® Tablets / Suspension / Drops
(Clarithromycin)

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

COMPOSITION:
Rithmo© **250mg Tablets**
Each film coated tablet contains:
Clarithromycin USP……..…… 250mg

Rithmo© **500mg Tablets**
Each film coated tablet contains:
Clarithromycin USP……..…… 500mg

Rithmo© **125mg/5ml Suspension**
Each 5ml of reconstituted suspension contains:
Clarithromycin Granules MS
equivalent to Clarithromycin USP……..…… 125mg

Rithmo© **250mg/5ml Suspension**
Each 5ml reconstituted suspension contains:
Clarithromycin Granules MS
equivalent to Clarithromycin USP……..…… 250mg

Rithmo© **125mg/5ml Drops**
Each 5ml reconstituted suspension contains:
Clarithromycin Granules MS
equivalent to Clarithromycin USP…..…… 125mg

CLINICAL PHARMACOLOGY:
Mode of Action
Clarithromycin prevents bacteria from growing, by interfering with their protein synthesis. Clarithromycin binds to the subunit 50S of the bacterial ribosome, and thus inhibits the translocation of peptides, resulting in inhibition of protein synthesis

Pharmacokinetics
Clarithromycin is rapidly absorbed from the gastrointestinal tract following oral administration, and under goes first pass metabolism; the bioavailability of the parent drug is about 55%. The extent of absorption is relatively unaffected by the presence of food. Peak concentration of clarithromycin and its active metabolite, 14-hydroxyclarithromycin, are reported to be about 0.6 and 0.7µg/ml respectively following a single 250mg dose by mouth; at steady-state the same dose given every 12 hours as tablets produces peak concentration of clarithromycin of about 1µg/ml
The drug and its principal metabolite are widely distributed, and tissue concentrations exceed those in serum, in part because of intracellular uptake. Clarithromycin is extensively metabolized in liver and excreted in feces via the bile. Substantial amounts are excreted in urine; at steady state about 20% and 30% respectively of a 250mg or 500mg dose is excreted in this way as unchanged drug.14-Hydroxyclarithromycin as well as other metabolites are also excreted in the urine accounting to 10 to 15% of the dose. The terminal half-life of clarithromycin is reportedly about 3 to 4 hours in patients receiving 250mg doses twice daily, and about 5 to 7 hours in those receiving 500mg twice daily. The half life is prolonged in renal impairment
Microbiology
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 (TWAR)
Mycobacteria
Mycobacterium avium complex [MAC] (consisting of:
Mycobacterium avium
Mycobacterium intracellulare)
Helicobacter
Helicobacter pylori

INDICATIONS AND USAGE:
Rithmo© (Clarithromycin) is indicated for the treatment of mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions as listed below:
Pharyngitis/Tonsillitis due to Streptococcus pyogenes
Acute otitis media in children
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 pneumonia due to Haemophilus influenzae, Mycoplasma pneumoniae, Streptococcus pneumoniae, or Chlamydia pneumoniae (TWAR)
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
For eradication of H. pylori ***Rithmo***© (Clarithromycin) tablets in combination with acid suppressants is also indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease

CONTRAINDICATIONS:
Clarithromycin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, or any of the macrolide antibiotics
Concomitant administration of clarithromycin and any of the following drugs is contraindicated: Cisapride, pimozide, astemizole, terfenadine, and ergotamine or dihydroergotamine

WARNING:
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 matabolized by CYP3A4 (e.g., verapamil, amlodipine, diltiazem)

DOSAGE:
Adults:
Pharyngitis/Tonsillitis
Due to S. pyogenes
The recommended dosage of clarithromycin is 250mg b.i.d. for 10 days
Acute maxillary sinusitis
Due to H. influenzae, M. catarrhalis and S. pneumoniae
The recommended dosage of clarithromycin is 500mg b.i.d. for 10 days
Acute exacerbation of chronic bronchitis
Due to H. influenzae

The recommended dosage of clarithromycin is 500mg b.i.d for 7 to 14 days
Due to M. catarrhalis and S. pneumoniae
The recommended dosage of clarithromycin is 250mg b.i.d. for 7 to 14 days

Community Acquired pneumonia
Due to H. influenzae
The recommended dosage of clarithromycin is 250mg b.i.d. for 7 days
Due to S. pneumoniae, C. pneumoniae & M. pneumoniae
The recommended dosage of clarithromycin is 500mg b.i.d. for 7 to 14 days
Uncomplicated skin and skin structure infections
Due to S. aureus and S. pyogenes
The recommended dosage of clarithromycin is 250mg b.i.d. for 7 to 14 days

120 mm

210 mm

Children:
The usual recommended dosage of ***Rithmo***© (Clarithromycin) is 7.5mg/kg twice daily upto a maximum of 500mg twice daily. The usual duration of treatment is for 5-10 days depending on the pathogen involved and severity of the condition

Paediatric Dosage Guidelines (based on body weight)			
Weight in kg	**Dosage in mg**	**Dosage in ml** 125mg/5ml Suspension & Drops	**Dosage in ml** 250mg/5ml Suspension
8 - 11	62.5mg b.i.d.	2.5ml (1/2 tsp b.i.d.)	1.25ml (1/4 tsp b.i.d.)
12 -19	125mg b.i.d.	5ml (1 tsp b.i.d.)	2.5ml (1/2 tsp b.i.d.)
20 - 29	187.5mg b.i.d.	7.5ml (1 1/2 tsp b.i.d.)	3.75ml (3/4 tsp b.i.d.)
30 - 40	250mg b.i.d.	10ml (2 tsp b.i.d.)	5ml (1 tsp b.i.d.)

*Children <8kg should be based on a per kg basis (approx. 7.5mg/kg b.i.d.)

Hepatic and renal impairment: Clarithromycin may be administered without dosage adjustment in the presence of hepatic impairment if there is normal renal function. However, in the presence of severe renal impairment (CRCL 30 to 60ml/min), with or without coexisting hepatic impairment, the dose should be halved or the dosing interval doubled. For patients with CRCL < 30ml/min, the dose of clarithromycin should be decreased by 75%

OR
As directed by the physician

DIRECTION FOR RECONSTITUTION:
Rithmo© **125mg/5ml Suspension (60ml)**
Shake bottle to loosen the mass. Add one time completely filled provided cup (30ml) with freshly boiled cool water into bottle. Shake slowly clockwise ↻ to form uniform suspension

Rithmo© **250mg/5ml Suspension (70ml)**
Shake bottle to loosen the mass. Add two times completely filled provided cup (27ml) with freshly boiled cool water into bottle. Shake slowly clockwise ↻ to form uniform suspension

Rithmo© **125mg/5ml Drops (25ml)**
Shake bottle to loosen the mass. Add one time completely filled provided cup (18ml) with freshly boiled cool water into bottle. Shake slowly clockwise ↻ to form uniform suspension

PRECAUTION:
Pregnancy
Teratogenic Effects. Pregnancy Category C
There are no adequate and well-controlled studies in pregnant women. Clarithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Nursing Mothers
Caution should be exercised when clarithromycin is administered to a nursing woman. It is known that clarithromycin is excreted in the milk of lactating animals and that other drugs of this class are excreted in human milk

STABILITY:
See expiry on the pack

PRESENTATION:
Rithmo© 250mg tablets in blister pack of 10's
Rithmo© 500mg tablets in blister pack of 10's
Rithmo© 125mg/5ml suspension in pack of 60ml
Rithmo© 250mg/5ml suspension in pack of 70ml
Rithmo© 125mg/5ml drops in pack of 25ml

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30°C
Improper storage may deteriorate the medicine

The reconstituted suspension should be kept at room temperature, so that potency of the product remains stable and be used within 14 days. Do not refrigerate the reconstituted suspension

رِتھمو ٹیبلٹ/سسپینشن/ڈراپس
(کلیرتھرومائی سن)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی
تیار شدہ سسپینشن کو کمرے کے درجہ حرارت پر رکھیں تا کہ دوا کی تاثیر برقرار رہے
اور ۱۴ یوم کے اندر استعمال کرلیں۔ تیار شدہ دوا ریفریجریٹر میں نہ رکھیں

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

Rithmo®-XL 500mg Tablets

(Clarithromycin)

Extended Release

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

COMPOSITION:

Rithmo®-XL 500mg tablets

Each extended release film coated tablet contains:

Clarithromycin USP…….. 500mg

CLINICAL PHARMACOLOGY:

Mode of Action

Clarithromycin prevents bacteria from growing, by interfering with their protein synthesis. Clarithromycin binds to the subunit 50S of the bacterial ribosome, and thus inhibits the translocation of peptides, resulting in inhibition of protein synthesis

Pharmacokinetics

Clarithromycin extended-release tablets provide extended absorption of clarithromycin from the gastrointestinal tract after oral administration. Relative to an equal total daily dose of immediate release clarithromycin tablets, clarithromycin extended-release tablets provide lower and later steady state peak plasma concentrations but equivalent 24-hours AUC's for both clarithromycin and its microbiologically-active metabolite, 14-hydroxy clarithromycin. While the extent of formation of 14-hydroxy clarithromycin following administration of clarithromycin extended release tablets is not affected by food, administration under fasting conditions is associated with approximately 30% lower clarithromycin AUC relative to administration with food. Therefore, clarithromycin extended release tablets should be taken with food

In healthy human subjects, steady-state peak plasma clarthromycin concentrations of approximately 2 to 3µg/ml were achieved about 5 to 8 hours after oral administration of 2 x 500mg clarithromycin extended release tablets once daily; for 14-hydroxy clarithromycin, steady-state peak plasma concentrations of approximately 0.8µg/ml were attained about 6 to 9 hours after dosing. Steady-state peak plasma clarithromycin concentrations of approximately 1 to 2µg/ml were achieved about 5 to 6 hours after oral administration of a single 500mg clarithromycin extended release tablet once daily; for 14-hydroxy clarithromycin, steady state peak plasma concentrations of approximately 0.6µg/ml were attained about 6 hours after dosing

Microbiology

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
Neisseria gonorrhoeae
Legionella pneumophila

Other microorganisms

Mycoplasma pneumoniae
Chlamydia pneumoniae **(TWAR)**

Mycobacteria

Mycobacterium avium complex [MAC] (consisting of: Mycobacterium avium, Mycobacterium intracellulare)

Helicobacter

Helicobacter pylori

INDICATIONS AND USAGE:

Rithmo®-XL (Clarithromycin) is indicated for the treatment of:

- Lower respiratory tract infections (e.g., bronchitis, pneumonia)
- Upper respiratory tract infections (e.g., pharyngitis, sinusitis), and
- Skin and soft tissue infections (e.g., folliculitis, cellulitis, erysipelas)

CONTRAINDICATIONS:

Clarithromycin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, or any of the macrolide antibiotics Concomitant administration of clarithromycin and any of the following drugs is contraindicated: cisapride, pimozide, astemizole, terfenadine, and ergotamine or dihydroergotamine As the dose cannot be reduced from 500mg once-daily, ***Rithmo®-XL*** tablet is contraindicated in patient with creatinine clearanace less than 30ml/min. ***Rithmo®*** immediate release tablets may be utilized in this patient population

WARNING:

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 matabolized by CYP3A4 (e.g., verapamil, amlodipine, diltiazem)

DOSAGE AND ADMINISTRATION:

The usual recommended dosage of ***Rithmo®-XL*** (Clarithromycin) tablets in adults is 500mg once-daily with food. In more severe infections, the dose may be increased to 1000mg once daily (2x500mg). The usual duration of therapy is 5 to 14 days, excluding treatment of community acquired pneumonia and sinusitis which require 6 to 14 days therapy

OR

As directed by the physician

210mm

120mm

PRECAUTION:

Pregnancy

Teratogenic Effects. Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Clarithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Nursing Mothers

Caution should be exercised when clarithromycin is administered to a nursing woman. It is known that clarithromycin is excreted in the milk of lactating animals and that other drugs of this class are excreted in human milk

PRESENTATIONS:

Rithmo-XL 500mg tablets in a pack of 5's

STABILITY:

See expiry on the pack

INSTRUCTION:

To be swallowed whole with water

Keep out of reach of children

Avoid exposure to heat, light and humidity

Store between 15 to 30°C

Improper storage may deteriorate the medicine

رتھمو۔ ایکسایل

(کلیرتھرومائی سن)

۵۰۰ ملی گرام ٹیبلٹ

ایکسٹنڈڈ ریلیز

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ثابت ٹیبلٹ چبائے بغیر پانی سے نگل لیں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

210mm

120mm

Rithmo® 500mg Lyophilized Injection

(Clarithromycin Lactobionate)

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

COMPOSITION:
Rithmo® 500mg Lyophilized Injection
Each vial contains:
Clarithromycin Lactobionate equivalent to
Clarithromycin USP.....…… 500mg

CLINICAL PHARMACOLOGY:
Mode of Action: Clarithromycin prevents bacteria from growing, by interfering with their protein synthesis. Clarithromycin binds to the subunit 50S of the bacterial ribosome, and thus inhibits the translocation of peptides, resulting in inhibition of protein synthesis

Pharmacokinetics: The mean terminal phase half-life of parent drug was dose-dependent and ranged from 3.8 hours after the 500mg dose to 4.5 hours after the 1000mg dose (60 minutes infusion). The mean estimated plasma half-life for the 14-hydroxy metabolite showed some dose-dependent increase on higher doses and ranged from 7.3 hours after the 500mg dose to 9.3 hours after the 1000mg dose (60 minutes infusion)
The pharmacokinetics of clarithromycin and the 14-hydroxy metabolite are non-linear; steady state is achieved by day 3 of I.V. dosing. Following a single 500mg I.V. dose over 60 minutes, about 33% clarithromycin and 11% 14-hydroxy clarithromycin is excreted in the urine at 24 hours

Microbiology: 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 (TWAR)

Mycobacteria:
- Mycobacterium avium complex [MAC] consisting of:
- Mycobacterium avium
- Mycobacterium intracellulare
- Mycobacterium chelonae
- Mycobacterium fortuitum
- Mycobacterium kansasii

Helicobacter:
Helicobacter pylori

INDICATIONS AND USAGE:
Rithmo® I.V. is indicated whenever parenteral therapy is required for treatment of sensitive microorganisms in the following conditions:
- Upper respiratory tract infections
- Lower respiratory tract infections
- Skin and soft tissues infections
- Disseminated or localized mycobacterial infections due to Mycobacterium avium or Mycobacterium intracellulare. Localized infections due to Mycobacterium chelonae, Mycobacterium fortuitum, or Mycobacterium kansasii

CONTRAINDICATIONS:
Clarithromycin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, or any of the macrolide antibiotics

WARNINGS:
Cardiovascular events include prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia and torsade de pointes, have been seen in treatment with macrolides including clarithromycin. Therefore as the following situations may lead to an increased risk for ventricular arrhythmias (including torsade de pointes), clarithromycin should be used with caution in the following patients:

- Patients with coronary artery disease, severe cardiac insufficiency, conduction disturbances or clinically relevant bradycardia
- Patients with electrolyte disturbances such as hypomagnesaemia. Clarithromycin must not be given to patients with hypokalaemia
- Patients concomitantly taking other medicinal products associated with QT prolongation

DRUG INTERACTIONS:
Concomitant administration of clarithromycin and any of the following drugs is contraindicated: cisapride, pimozide, astemizole, terfenadine, and ergotamine or dihydroergotamine. Concomitant use of clarithromycin with lovastatin and simvastatin is contraindicated

SPECIAL WARNINGS:
Pregnant women should not be prescribed clarithromycin without carefully weighing the benefits against risk, particularly during the first three months of pregnancy
Caution is advised in patients with severe renal insufficiency
Due to the risk for QT prolongation, clarithromycin should be used with caution in patients with coronary artery disease, severe cardiac insufficiency, hypomagnesaemia, bradycardia (<50 bpm), or when coadministered with other medicinal products associated with QT prolongation

DOSAGE AND ADMINISTRATION:
The recommended dosage of clarithromycin I.V. is 1g daily, divided in two equal doses, each infused after further dilution with an appropriate I.V. diluent, over a 60 minutes time, there are no data supporting I.V. use of clarithromycin in children. Clarithromycin should not be given as a bolus or by intramuscular injection

I.V. therapy may be limited for up to 2 to 5 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 30mL/min, the dosage of clarithromycin should be reduced to one half of the normal recommended dose

The final solution for infusion is prepared as follow:
Step 1. Preparation of the vial solution: Inject 10ml of sterile water for injection into a vial containing the product. Shake until the vial contents have dissolved. Use only water for injection for the dissolution. Other solvents may result in the formation of a precipitate. Do not use solutions of inorganic salts or solutions containing preservatives. The reconstituted solution is stable for 24 hours at room temperature or for 48 hours in refrigerator
Parenteral drug products should be inspected visually for particulate matter prior to administration. If particulate matter is evident in reconstituted fluids, the drug solution should be discarded

Step 2. Preparation of infusion solution: Make up 10ml of the vial solution prepared in step 1 (containing 500mg clarithromycin) to 250ml using one of the following solutions:
- 0.9% Sodium Chloride
- 5% Dextrose
- 5% Dextrose in 0.3% Sodium Chloride
- 5% Dextrose in 0.45% Sodium Chloride
- 5% Dextrose in Ringer's lactate solution and Ringer's lactate solution

Store the solution for 6 hours at room temperature or 48 hours in refrigertor

Important: Both diluent steps (1 and 2) should be completed before use

PRECAUTION:
Pregnancy: There are no adequate and well-controlled studies in pregnant women. Clarithromycin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Nursing Mothers: Caution should be exercised when clarithromycin is administered to a nursing woman. It is known that clarithromycin is excreted in the milk of lactating animals as that other drugs of this class are excreted in human milk

PRESENTATIONS:
Rithmo® 500mg Lyophilized Injection in a pack of 1 vial + 10ml sterile water for injection

STABILITY:
See expiry on the pack

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store between 15 to 30°C
Improper storage may deteriorate the medicine

رِتھمو ۵۰۰ ملی گرام لائیوفلائیزڈ انجکشن

(کلیرتھرومائی سن لیکٹوبائیونیٹ)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ
کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی
تیار شدہ انجکشن کمرے کے درجہ حرارت پر ۲۴ گھنٹے یا ریفریجریٹر میں ۴۸ گھنٹے تک رکھنے کی صورت میں
قابل استعمال رہتا ہے جبکہ diluted محلول کمرے کے درجہ حرارت پر ۶ گھنٹے یا ریفریجریٹر میں ۴۸ گھنٹے
رکھنے کی صورت میں قابل استعمال رہتا ہے۔

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

R.N-02/HA/12/18