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# MOLOX®

(Moxifloxacin)

Tablet & Infusion

مولوکس

**COMPOSITION:**
***Molox Tablet 400 mg:***
Each film coated tablet contains:
Moxifloxacin HCl USP equivalent to
Moxifloxacin ..... 400 mg.

**Products Specs.:** USP

***Molox Infusion 400 mg/250 ml:***
Each 250 ml vial contains:
Moxifloxacin HCl BP equivalent to
Moxifloxacin ..... 400 mg.

**Products Specs.:** CCL Pharmaceuticals

**DESCRIPTION:**
Molox belongs to fluoroquinolone class of antibiotics. Moxifloxacin is bactericidal and its mode of action involves inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division. This mechanism is lethal to susceptible bacteria. Moxifloxacin is often referred to as a chemotherapeutic drug because its mode of action has so far not been noted in any natural occurring or semi-synthetic antibiotic.

**INDICATIONS:**
***Moxifloxacin is used to treat respiratory infections including:***
***Acute sinusitis caused by:*** H. influenzae, M. catarrhalis, S. pneumoniae.
***Acute exacerbations of chronic bronchitis caused by:*** H. influenzae, H. parainfluenzae, K. pneumoniae, M. catarrhalis, S. aureus, S. pneumoniae.

- Community-acquired pneumonia of Mild to Moderate Severity caused by: C. pneumoniae, H. influenzae, M. catarrhalis, M. pneumoniae, S. pneumoniae.
- Community-acquired pneumonia (CAP), including CAP caused by multi-drug resistant Streptococcus pneumoniae.
- Moxifloxacin is used to treat complicated skin and skin structure infections caused by methicillin susceptible Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, or Enterobacter cloacae and Uncomplicated Skin and Skin Structure Infections caused by methicillin-susceptible Staphylococcus aureus or Streptococcus pyogenes.
  Moxifloxacin is used to treat complicated Intra-Abdominal Infections including polymicrobial infections such as abscess caused by Escherichia coli, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus, Enterococcus faecalis, Proteus mirabilis, Clostridium perfringens, Bacteroides thetaiotaomicron, or Peptostreptococcus species.
- Moxifloxacin is used as a second-line agent in tuberculosis and may potentially have benefits in reducing treatment duration from its current six month to four months.
- Multi-drug resistant S. pneumoniae includes isolates previously known as PRSP (Penicillin-resistant S. pneumoniae), and are strains resistant to 2 or more of the following antibiotics: penicillin (MIC≥2 µg/mL), 2nd generation cephalosporins (e.g., cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to Moxifloxacin. Molox infusion is indicated for the treatment of adult > 18 years of age.

**PHARMACOKINETICS:**
***Absorption:*** Moxifloxacin, given as an oral tablet, is well absorbed from the gastrointestinal tract. The absolute bioavailability of Moxifloxacin is approximately 91 percent. Co-administration with a high fat meal (i.e., 500 calories from fat) does not affect the absorption of Moxifloxacin.
***Distribution:*** Moxifloxacin is approximately 45% bound to serum proteins, independent of drug concentration. The volume of distribution of Moxifloxacin ranges from 1.7 to 2.7 L/kg. Moxifloxacin is widely distributed throughout the body, with tissue concentrations often exceeding plasma concentrations. Moxifloxacin has been detected in the saliva, nasal and bronchial secretions, mucosa of the sinuses, skin blister fluid, subcutaneous tissue, skeletal muscle, and abdominal tissues and fluids following oral administration of 400mg.
***Metabolism:*** Moxifloxacin is metabolized via glucuronide and sulfate conjugation. The sulfate conjugate (M1) accounts for approximately 38% of the dose, and is eliminated primarily in the feces. Approximately 14% of an oral dose is converted to a glucuronide conjugate (M2), which is excreted exclusively in the urine. Peak plasma concentrations of M2 are approximately 40% those of the parent drug, while plasma concentrations of M1 are generally less than 10% those of Moxifloxacin. The sulfate (M1) and glucuronide (M2) conjugates are not microbiologically active.
***Elimination:***
Approximately 45% of an oral dose of Moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in feces).
A total of 96%±4% of an oral dose is excreted as either unchanged drug or known metabolites. The mean (±SD) apparent total body clearance and renal clearance are 12 ±2.0 L/hr and 2.6 ±0.5 L/hr, respectively.

**DOSAGE AND ADMINISTRATION:**
The recommended dose for Molox tablet is 400 mg once-daily for all indications.
***Duration of treatment:***
The duration of treatment should be determined by the severity of the indication or clinical response. In general, antibiotic therapy should be used for 3-4 days after the manifestations of the infection have cleared. The duration of therapy depends on the type of infection as described below.

| Infection | Daily Dose | Duration (Tablet) | Duration (Infusion) |
|---|---|---|---|
| Acute Bacterial Sinusitis | 400 mg | 7 days | 7 days |
| Acute Bacterial Exacerbation of Chronic Bronchitis | 400 mg | 5 days | 5 days |
| Community Acquired Pneumonia | 400 mg | 10 days | 7-14 days |
| Uncomplicated Skin and Skin Structure Infections | 400 mg | 7 days | |
| Complicated Skin and Skin Structure Infections | 400 mg | 7-21 days | |
| Complicated Intra-Abdominal Infections | 400 mg | 5-14 days | |

In case of community acquired pneumonia the recommended total treatment duration for sequential administration (intravenous followed by oral) is 7-14 days.
The recommended duration of treatment in skin and soft tissue infections with Molox infusion is 7 days. Therapy may be initial intravenous administration, followed by oral tablet administration when clinically indicated.
Moxifloxacin is administered orally, independent of meals. The tablets are swallowed whole. Patients should be advised to drink fluids liberally and take Moxifloxacin at least 4 hours before or 8 hours after antacids containing magnesium, aluminium, or calcium or multivitamins containing iron or zinc.
***Method of administration:***
The infusion solution should be infused intravenously over 60 minutes. It can be administered directly or together with compatible infusion solution.
The following co-infusions were found to form stable mixtures over a period of 24 hours at room temperature with Moxifloxacin infusion solution, and can therefore be considered as compatible:
Water for injection, Sodium Chloride 0.9%, Sodium Chloride 1 molar, Glucose 5%, Glucose 10%, Glucose 40%, Xylit 20%, Ringer solution, Lactated ringer solution, Aminofusin 10%, Jonosteril D5.
If Moxifloxacin infusion solution is to be given with another drug,each drug should be given separately.
**Special Populations:**
***Elderly:*** No adjustment of dosage is required in the elderly.

***Children:*** The use of Moxifloxacin in children and adolescents in the growth phase is contra-indicated.

***Hepatic impairment:*** No dosage adjustment is required in patients with slightly impaired liver function. Moxifloxacin is not recommended in patients with moderate or severe hepatic impairment.
***Renal impairment:*** No dose adjustment is required in patients with any degree of renal impairment (including creatinine clearance ≤30 mL/min/1,73m²). Moxifloxacin should therefore not be used in patients with advanced renal impairment.
***Interethnic differences:*** No adjustment of dosage is required in ethnic groups.
***Gender:*** Dosage adjustments based on gender are not necessary.

**CONTRAINDICATIONS**

- Known hypersensitivity to Moxifloxacin,other Quinolones, or any other ingredient of the preparation.
- Patients with history of tendon disorder related to Quinolone treatment
- Documented QT prolongation.

**WARNINGS**
***Cardiac Effects:***
**QT Interval Prolongation**
Moxifloxacin has been shown to prolong the QT interval of the ECG in some patients. The drug should be avoided in patients with known prolongation of the QT interval, patients with hypokalemia and patients receiving Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic agents, due to the lack of clinical experience with the drug in these patient populations and the potential risk.
***CNS and Psychiatric Effects:***
Convulsions, increased intracranial pressure and toxic psychosis have been reported in patients receiving quinolones, including Moxifloxacin, may also cause CNS stimulation which may lead to abnormal dreams, agitation, anxiety, confusion, depression, dizziness, emotional lability, hallucinations, insomnia, lightheadedness, nervousness, nightmares, paranoia, restlessness and tremors. These reactions may occur after the first dose.
***Chondrotoxic Effects:***
As with other members of the quinolone class, Moxifloxacin has caused arthropathy and/or chondrodysplasia in immature dogs. The significance of these findings to humans is unknown.
***Hypersensitivity:***
Serious hypersensitivity and/or anaphylactic reactions have been reported in patients receiving quinolone therapy,

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including Moxifloxacin. Moxifloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity.
***Musculoskeletal Effects:***
Ruptures of the shoulder, hand and Achilles tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones. Moxifloxacin should be discontinued if the patient experiences pain, inflammation or rupture of a tendon.
***Pseudomembranous Colitis:***
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Moxifloxacin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

**PRECAUTIONS:**
***Geriatrics:*** There is no difference in the safety of Moxifloxacin in patients aged 65 or older compared to younger adults.
***Children:*** The safety and efficacy of Moxifloxacin in pediatric populations less than 18 years of age have not been established.
***Pregnancy:*** Moxifloxacin should not be used in pregnant women unless the potential benefits outweigh the potential risk to the fetus.
***Lactation:*** Moxifloxacin may also be excreted in human milk. A decision should be made to either discontinue nursing or discontinue the administration of Moxifloxacin, taking into account the importance of Moxifloxacin therapy to the mother and the possible risk to the infant.
***Carcinogenesis, Mutagenesis, Impairment of Fertility:*** Long term studies in animals to determine the carcinogenic potential of Moxifloxacin have not been performed. In studies conducted on animals, Moxifloxacin was found to be non mutagenic and have no effect on fertility in male and female.
***Phototoxicity:*** Phototoxicity has been reported in patients receiving certain quinolones. The patient should be advised to avoid excessive sunlight or artificial ultraviolet light during treatment with Moxifloxacin.

**SIDE EFFECTS:**
**The following side effects may occur:**
***Cardiovascular:*** Palpitation, QT prolongation, tachycardia, vasodilation.
Central nervous system: Anxiety, chills, dizziness (2%), headache, insomnia, malaise, nervousness, pain, somnolence, tremor, vertigo.
***Dermatologic:*** Dry skin, pruritus, rash (maculopapular, purpuric, pustular).
Endocrine & metabolic: Serum chloride increased (2%), serum ionized calcium increased (2%), serum glucose decreased (2%).
***Gastrointestinal:*** Abdominal pain, amylase increased, amylase decreased (2%), anorexia, constipation, dry mouth, dyspepsia, flatulence, glossitis, lactic dehydrogenase increased, stomatitis, taste perversion, vomiting.
***Genitourinary:*** Vaginal moniliasis, vaginitis
***Hematologic:*** Eosinophilia, leukopenia, prothrombin time prolonged, increased INR, thrombocythemia.
Increased serum levels of the following (2%): MCH, neutrophils, WBC.
Decreased serum levels of the following (2%): Basophils, eosinophils, hemoglobin, RBC, neutrophils.
***Hepatic:*** Bilirubin decreased or increased (2%), GGTP increased, liver function test abnormal.
Neuromuscular & skeletal: Arthralgia, myalgia, weakness.
***Renal:*** Serum albumin increased (2%).
***Respiratory:*** Pharyngitis, pneumonia, rhinitis, sinusitis, $pO_2$ increased (2%).
***Miscellaneous:*** Allergic reaction, infection, diaphoresis, oral moniliasis.

**DRUG INTERACTIONS:**
***Antacids, Sucralfate, Metal Cations, Multivitamins:***
Oral administration of quinolones with antacids containing aluminium or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, may substantially interfere with the absorption of Quinolones. Therefore, Moxifloxacin should be taken at least 4 hours before or 8 hours after these agents.
No clinically significant drug-drug interactions between itraconazole, theophylline, warfarin, digoxin, atenolol, oral contraceptives or glyburide have been observed with Moxifloxacin. Itraconazole, theophylline, digoxin, probenecid, morphine, ranitidine, and calcium have been shown not to significantly alter the pharmacokinetics of Moxifloxacin.
***Warfarin:***
Quinolones, including Moxifloxacin, have been reported to enhance the anticoagulant effects of warfarin or its derivatives in the patient population.
***Drugs metabolized by Cytochrome P450 enzymes:***
In vitro studies with cytochrome P450 isoenzymes (CYP) indicate that Moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2, suggesting that Moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these enzymes.
***Nonsteroidal anti-inflammatory drugs (NSAIDs):***
The concomitant administration of a nonsteroidal anti-inflammatory drug with a quinolone may increase the risks of CNS stimulation and convulsions.

**OVERDOSAGE:**
**Symptoms:** Toxic signs after administration of a single high dose of Moxifloxacin in animals included CNS and gastrointestinal effects.
**Treatment:** In the event of acute overdosage, the stomach should be emptied. ECG monitoring is recommended due to the possible prolongation of the QT interval. Adequate hydration must be maintained. Concomitant administration of charcoal with a dose of 400 mg oral or intravenous Moxifloxacin will reduce systemic availability of the drug by more than 80% or 20% respectively. The application of charcoal may be useful to prevent excessive increase of systemic exposure to Moxifloxacin in cases of oral overdose.

**INSTRUCTIONS:**
***For Tablet:***
- Store below 30°C.
***For Infusion:***
- Store at 15°C-30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on prescription of registered medical practitioner.

**PRESENTATION:**

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| **Molox Tablet 400 mg** | : | Pack of 1 x 5 tablets. |
| **Molox Infusion 400 mg/250 ml** | : | Pack of 1 x 250 ml vial. |

**ہدایات:**
ٹیبلٹ: ۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
انفیوژن: ۱۵-۳۰ درجہ سینٹی گریڈ پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

*FOR FURTHER INFORMATION PLEASE CONTACT:*

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