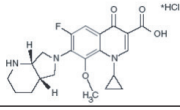
ASPIMOX™
(Moxifloxacin)

ایس پی موکس

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated tablet contains:
Moxifloxacin Hydrochloride (USP) equivalent to
Moxifloxacin.....400 mg

DESCRIPTION
Aspimox (Moxifloxacin) is a synthetic broad spectrum antibacterial agent for oral administration. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt of 1-cyclopropyl-7-[(S,S) 2,8-diazabicyclo[4.3.0] non-8-yl]-6-fluoro-8- methoxy-1,4-dihydro -4-oxo-3 quinoline carboxylic acid. Its empirical formula is $C_{21}H_{24}FN_3O_4$. HCl and it has a molecular weight of 437.9. Its chemical structure is as follows



WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYTEM EFFECTS AND EXACERBATION OF MYASTHENIA GRAVIS

- Fluoroquinolones, including Moxifloxacin, is known to be associated with disabling and potentially irreversible serious adverse reactions that occur together, including:
  - Tendinitis and tendon rupture
  - Peripheral neuropathy
  - Central nervous system effects

Discontinue Moxifloxacin immediately and avoid the use of Fluoroquinolones, including Moxifloxacin, in patients who experience any of these serious adverse reactions

- Fluoroquinolones, including Moxifloxacin, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid Moxifloxacin in patients with known history of myasthenia gravis
- Because Fluoroquinolones, including Moxifloxacin, is known to be associated with serious adverse reactions, reserve Moxifloxacin for use in patients who have no alternative treatment options for the following indications:
  - Acute bacterial sinusitis
  - Acute bacterial exacerbation of chronic bronchitis

CLINICAL INFORMATION
Indications
Aspimox (Moxifloxacin) Tablets are indicated for the treatment of following bacterial infections:
- Acute bacterial sinusitis.
- Acute bacterial exacerbation of chronic bronchitis.
- Community acquired pneumonia.
- Un-complicated skin and skin structure infections.
- Complicated skin and skin structure infections
- Plague (pneumonic and septicemic plague)

Dosage and Administration
The dose of Aspimox (Moxifloxacin) is 400 mg orally once every 24 hours. The duration of therapy depends on the type of infection as described in the Table below.

Type of Infection [a]	Dose Every 24 hours	Duration (days) [b]
Community Acquired Pneumonia	400 mg	7-14
Uncomplicated Skin and Skin Structure Infections (SSSI)	400 mg	7
Complicated SSSI	400 mg	7-21
Complicated Intra-Abdominal Infections	400 mg	5-14
Plague[c]	400 mg	10-14
Acute Bacterial Sinusitis (ABS)	400 mg	10
Acute Bacterial Exacerbation of Chronic Bronchitis (ABECB)	400 mg	5

a)Due to the designated pathogens.
b)Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.
c)Drug administration should begin as soon as possible after suspected or confirmed exposure to Yersinia pestis.

Dosage Requirement
Aspimox (Moxifloxacin) Tablets can be taken with or without food, drink fluids liberally.

Contraindication
Moxifloxacin is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antibacterials.
Pregnancy and lactation.
Patients below 18 years of age.

Warnings and Precautions
Disabling and potentially irreversible serious adverse reactions including tendinitis and tendon rupture, peripheral neuropathy, and central nervous system effects
Fluoroquinolones, including Moxifloxacin, is known to be associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions can occur within hours to weeks after starting Moxifloxacin.
Patients of any age or without pre-existing risk factors are known to experience these adverse reactions. Discontinue Moxifloxacin immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including Moxifloxacin, in patients who experience any of these serious adverse reactions associated with fluoroquinolones.
Tendinitis and Tendon Rupture
Fluoroquinolones, including Moxifloxacin, are known to be associated with an increased risk of tendinitis and tendon rupture in all ages and adverse reactions. This adverse reaction most frequently involves the Achilles tendon, and is also known to occur with the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendons. Tendinitis or tendon rupture can occur within hours or days of starting moxifloxacin or as long as several months after completion of therapy.
Discontinue Moxifloxacin immediately if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug. Avoid fluoroquinolones, including Moxifloxacin; in patients who have a history of tendon disorders or who have experienced tendinitis or tendon rupture.
Peripheral Neuropathy
Fluoroquinolones, including Moxifloxacin, are known to be associated with an increased risk of peripheral neuropathy. Sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness are known to occur in patients receiving fluoroquinolones including Moxifloxacin.
Discontinue Moxifloxacin immediately if the patient experiences symptoms of peripheral neuropathy.
Central Nervous System Effects
Fluoroquinolones, including Moxifloxacin, are known to be associated with an increased risk of central nervous system (CNS) reactions, including: convulsions and increased intracranial pressure (including pseudotumor cerebri) and toxic psychosis, Fluoroquinolones may also cause CNS reactions of nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression, and, suicidal thoughts or acts. As with all fluoroquinolones, use Moxifloxacin when the benefits of treatment exceed the risks in patients with known or suspected CNS disorders.
Exacerbation of Myasthenia Gravis
Fluoroquinolones, including Moxifloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Avoid Moxifloxacin in patients with known history of myasthenia gravis.
QT Prolongation
Moxifloxacin is known to prolong the QT interval of the electrocardiogram in some patients. Avoid Moxifloxacin in patients with the following risk factors due to the lack of clinical experience with the drug in these patient populations:
- Known prolongation of the QT interval
- Ventricular arrhythmias including torsade de pointes because QT prolongation may lead to an increased risk for these conditions
- Ongoing proarrhythmic conditions, such as clinically significant

bradycardia and acute myocardial ischemia,
• Uncorrected hypokalemia or hypomagnesemia
• Class IA (for example, quinidine, procainamide) or Class III (for example, amiodarone, sotalol) antiarrhythmic agents
• Other drugs that prolong the QT interval such as cisapride, erythromycin, antipsychotics, and tricyclic antidepressants
In patients with mild, moderate, or severe liver cirrhosis, metabolic disturbances associated with hepatic insufficiency may lead to QT prolongation. Monitor ECG in patients with liver cirrhosis treated with Moxifloxacin.

Other Serious and Sometimes Fatal Adverse Reactions

Other serious and sometimes fatal adverse reactions, some due to hypersensitivity, and some due to uncertain etiology, are known to occur in patients receiving therapy with fluoroquinolones, including Moxifloxacin.
Discontinue Moxifloxacin immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and institute supportive measures.

Hypersensitivity Reactions

Serious anaphylactic reactions, some following the first dose, are known to occur in patients receiving fluoroquinolone therapy, including Moxifloxacin. Some reactions are accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Discontinue Moxifloxacin at the first appearance of a skin rash or any other sign of hypersensitivity.

Clostridium difficile-Associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) is known to occur with use of nearly all antibacterial agents, including Moxifloxacin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

Blood Glucose Disturbances

As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycemia and hyperglycemia are known to occur with Moxifloxacin. In diabetic patients, careful monitoring of blood glucose is recommended.

Photosensitivity/Phototoxicity

Moderate to severe photosensitivity/phototoxicity reactions, can be associated with the use of fluoroquinolones, including Moxifloxacin, after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Moxifloxacin should be discontinued if phototoxicity occurs.

Development of Drug Resistant Bacteria

Prescribing Moxifloxacin 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.

Interactions

Antacids, sucralfate, multivitamins and other products containing multivalent cations

Fluoroquinolones, including Moxifloxacin, form chelates with alkaline earth and transition metal cations. Oral administration of Moxifloxacin with antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, may substantially interfere with the absorption of Moxifloxacin, resulting in systemic concentrations considerably lower than desired. Therefore, Moxifloxacin should be taken at least 4 hours before or 8 hours after these agents.

Warfarin

Fluoroquinolones, including Moxifloxacin, are known to enhance the anticoagulant effects of warfarin or its derivatives in the patient population. In addition, infectious disease and its accompanying inflammatory process, age, and general status of the patient are risk factors for increased anticoagulant activity.

Antidiabetic agents

Disturbances of blood glucose, including hyperglycemia and hypoglycemia, are known to occur in patients treated concomitantly with fluoroquinolones, including Moxifloxacin, and an antidiabetic agent.

Nonsteroidal anti-inflammatory drugs

The concomitant administration of a nonsteroidal anti-inflammatory drug (NSAID) with a fluoroquinolone, including Moxifloxacin, may increase the risks of CNS stimulation and convulsions.

Drugs that Prolong QT

There is limited information available on the potential for a pharmacodynamic interaction in humans between Moxifloxacin and other drugs that prolong the QTc interval of the electrocardiogram. Therefore, Moxifloxacin should be avoided with Class IA and Class III antiarrhythmics

Pregnancy and Breastfeeding

The safety of moxifloxacin in human pregnancy is not evaluated. Due to the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of immature animals and reversible joint injuries described in children receiving some fluoroquinolones, moxifloxacin must not be used in pregnant women.
There is no data available in lactating or nursing women. Available data indicate that small amounts of moxifloxacin are secreted in milk, Therefore breast-feeding is contraindicated during moxifloxacin therapy.

Effects on ability to drive and use machines

No data on the effects of moxifloxacin on the ability to drive and use machines is evaluated. However, fluoroquinolones including moxifloxacin may result in an impairment of the patient's ability to drive or operate machinery due to CNS reactions. Patients should be advised to see how they react to moxifloxacin before driving or operating machinery.

Adverse Reactions

Blood and lymphatic system disorders - Agranulocytosis and Pancytopenia
Cardiac disorders - Ventricular tachyarrhythmias (including in very rare cases cardiac arrest and torsade de pointes, and usually in patients with concurrent severe underlying proarrhythmic conditions)
Ear and labyrinth disorders - Hearing impairment, including deafness (reversible in majority of cases)
Eye disorders - Vision loss (especially in the course of CNS reactions, transient in majority of cases)
Hepatobiliary disorders - Hepatitis (predominantly cholestatic) Hepatic failure (including fatal cases) Jaundice Acute hepatic necrosis
Immune system disorders - Anaphylactic reaction Anaphylactic shock Angioedema (including laryngeal edema)
Musculoskeletal and connective tissue disorders - Tendon rupture
Nervous system disorders - Altered coordination, abnormal gait, myasthenia gravis, muscle weakness and peripheral neuropathy (that may be irreversible), polyneuropathy
Psychiatric disorders - Psychotic reaction (very rarely culminating in self-injurious behavior, such as suicidal ideation/thoughts or suicide attempts
Renal and urinary disorders - Interstitial nephritis
Respiratory, thoracic and mediastinal disorders - Allergic pneumonitis
Skin and subcutaneous tissue disorders - Photosensitivity / phototoxicity reaction, stevens-johnson syndrome and toxic epidermal necrolysis.

Overdose

Single oral overdoses up to 2.8 g are not known to be associated with any serious adverse events. In the event of acute overdose, Empty the stomach and maintain adequate hydration. Monitor ECG due to the possibility of QT interval prolongation. Carefully observe the patient and give supportive treatment. The administration of activated charcoal as soon as possible after oral overdose may prevent excessive increase of systemic moxifloxacin exposure. About 3% and 9% of the dose of moxifloxacin, as well as about 2% and 4.5% of its glucuronide metabolite are removed by continuous ambulatory peritoneal dialysis and hemodialysis, respectively.

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Quinolone antibacterials, fluoroquinolones, ATC code: J01MA14

Mechanism of action

The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination.
Moxifloxacin is known to be active against most isolates of the following bacteria:

Gram-positive bacteria

Enterococcus faecalis, Staphylococcus aureus, Streptococcus anginosus, Streptococcus constellatus, Streptococcus pneumoniae (including multi-drug resistant isolates [MDRSP] **) and Streptococcus pyogenes.
**MDRSP, Multi-drug resistant *Streptococcus pneumoniae* includes isolates previously known as PRSP (Penicillin resistant *S.*

pneumoniae), and are isolates resistant to two or more of the following antibiotics: penicillin (MIC) ≥2 mcg/mL), 2nd generation cephalosporins (for example, cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

Gram-negative bacteria
Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumonia, Moraxella catarrhalis, Proteus mirabilis and Yersinia pestis
Anaerobic bacteria
Bacteroides fragilis, Bacteroides thetaiotaomicron, Clostridium perfringens and Peptostreptococcus species
Pharmacokinetic Properties
Absorption
Moxifloxacin, given as an oral tablet, is well absorbed from the gastrointestinal tract. The absolute bioavailability of moxifloxacin is approximately 90 percent. Co-administration with a high fat meal (that is, 500 calories from fat) does not affect the absorption of moxifloxacin.
Consumption of 1 cup of yogurt with moxifloxacin does not affect the rate or extent of the systemic absorption (that is, area under the plasma concentration time curve (AUC).
Distribution
Moxifloxacin is approximately 30–50% 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 is known to be 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 400 mg. The rates of elimination of moxifloxacin from tissues generally parallel the elimination from plasma.
Metabolism
Approximately 52% of an oral dose of moxifloxacin is metabolized via glucuronide and sulfate conjugation. The cytochrome P450 system is not involved in moxifloxacin metabolism, and is not affected by moxifloxacin. The sulfate conjugates (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.
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 L/hr and 2.6 ± 0.5 L/hr, respectively.

PHARMACEUTICAL INFORMATION
Shelf life
2 years.

Special Precautions for storage
Do not store above 30°C.
Protect from light and moisture.
Keep out of the reach of children.

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۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
دوا کو روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Nature and contents of container / Packaging
Aspimox (Moxifloxacin) 400 mg tablets are available in a blister pack of 5's (1x 5's).

MANUFACTURED BY:

ASPIN
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