Maroxi

(Moxifloxacin)

Broad Spectrum Antibiotic

مارو کسی ٹیبلیٹس

(موکسی فلاکساسن)

۴۰۰ ملی گرام ٹیبلیٹس

400mg Tablets

FULL PRESCRIBING INFORMATION

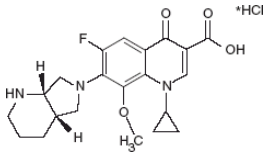
WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAI NERVOUS SYTEM EFFECTS and EXACERBATION OF MYASTHENIA GRAVIS

- **Fluoroquinolones, including MAROXI, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together [see Warnings and Precautions, including:**
  - **Tendinitis and tendon rupture [see Warnings and Precautions**
  - **Peripheral neuropathy [see Warnings and Precautions**
  - **Central nervous system effects [see Warnings and Precautions**

  Discontinue MAROXI immediately and avoid the use of fluoroquinolones, including MAROXI, in patients who experience any of these serious adverse reactions [see Warnings and Precautions.
- **Fluoroquinolones, including MAROXI, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid MAROXI in patients with known history of myasthenia gravis [see Warnings and Precautions.**
- **Because fluoroquinolones, including MAROXI, have been associated with serious adverse reactions [see Warnings and Precautions, reserve MAROXI for use in patients who have no alternative treatment options for the following indications:**
  - **Acute bacterial sinusitis [see Indications and Usage**
  - **Acute bacterial exacerbation of chronic bronchitis [see Indications and Usage**

1 DESCRIPTION

MAROXI (moxifloxacin) hydrochloride is a synthetic 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. It is a slightly yellow to yellow crystalline substance with a molecular weight of 437.9. Its empirical formula is $C_{21}H_{24}FN_3O_4$*HCl and its chemical structure is as follows:



COMPOSITION:

Maroxi Tablet

Each film coated tablet contains:

Moxifloxacin HCl eq. to Moxifloxacin...400 mg

(USP Specification)

2 INDICATIONS AND USAGE

2.1 Community Acquired Pneumonia

MAROXI is indicated in adult patients for the treatment of Community Acquired Pneumonia caused by susceptible isolates of Streptococcus pneumoniae (including multi-drug resistant Streptococcus pneumoniae [MDRSP]), Haemophilus influenzae, Moraxella catarrhalis, methicillin-susceptible Staphylococcus aureus, Klebsiella pneumoniae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae [see Clinical Studies.

MDRSP isolates are isolates resistant to two or more of the following antibacterial drugs: penicillin (minimum inhibitory concentrations [MIC] ≥ 2 mcg/mL), 2nd generation cephalosporins (for example, cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

2.2 Uncomplicated Skin and Skin Structure Infections

MAROXI is indicated in adult patients for the treatment of Uncomplicated Skin and Skin Structure Infections caused by susceptible isolates of methicillin-susceptible Staphylococcus aureus or Streptococcus pyogenes [see Clinical Studies.

2.3 Complicated Skin and Skin Structure Infections

MAROXI is indicated in adult patients for the treatment of Complicated Skin and Skin Structure Infections caused by susceptible isolates of methicillin-susceptible Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, or Enterobacter cloacae [see Clinical Studies].

2.4 Complicated Intra-Abdominal Infections

MAROXI is indicated in adult patients for the treatment of Complicated Intra-Abdominal Infections including polymicrobial infections such as abscess caused by susceptible isolates of Escherichia coli, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus, Enterococcus faecalis, Proteus mirabilis, Clostridium perfringens, Bacteroides thetaiotaomicron, or Peptostreptococcus species [see Clinical Studies].

2.5 Acute Bacterial Sinusitis

MAROXI is indicated in adult patients (18 years of age and older) for the treatment of acute bacterial sinusitis (ABS) caused by susceptible isolates of Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis [see Clinical Studies].

Because fluoroquinolones, including MAROXI, have been associated with serious adverse reactions [see Warnings and Precautions] and for some patients ABS is self-limiting, reserve MAROXI for treatment of ABS in patients who have no alternative treatment options.

2.6 Acute Bacterial Exacerbation of Chronic Bronchitis

MAROXI is indicated in adult patients for the treatment of Acute Bacterial Exacerbation of Chronic Bronchitis (ABECB) caused by susceptible isolates of Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, methicillin-susceptible Staphylococcus aureus, or Moraxella catarrhalis [see Clinical Studies].

Because fluoroquinolones, including MAROXI, have been associated with serious adverse reactions [see Warnings and Precautions] and for some patients ABECB is self-limiting, reserve MAROXI for treatment of ABECB in patients who have no alternative treatment options.

2.7 Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of MAROXI and other antibacterial drugs, MAROXI should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

3 DOSAGE AND ADMINISTRATION

3.1 Dosage in Adult Patients

The dose of MAROXI is 400 mg (orall) once every 24 hours. The duration of therapy depends on the type of infection as described in Table 1.

Table 1: Dosage and Duration of Therapy in Adult Patients

Type of Infection[a]	Dose Every 24 hours	Duration[b] (days)
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	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 [see Indications and Usage (1)].
b) Sequential therapy (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.

3.2 Important Administration Instructions

MAROXI Tablets

With Multivalent Cations

Administer MAROXI Tablets at least 4 hours before or 8 hours after products containing magnesium, aluminum, iron or zinc, including antacids, sucralfate, multivitamins and didanosine buffered tablets for oral suspension or the pediatric powder for oral solution [see Drug Interactions and Clinical Pharmacology].

With Food

MAROXI Tablets can be taken with or without food, drink fluids liberally.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Discard any unused portion because the premix flexible containers are for single-use only.

4 DOSAGE FORMS AND STRENGTHS

4.1 MAROXI Tablets

Appearance of coated Tablet Oblong Shape Light brown color tablet plain on one side & bisected line on the side.

5 CONTRAINDICATIONS

MAROXI is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of anti-bacterials [see Warnings and Precautions].

6 WARNINGS AND PRECAUTIONS

6.1 Disabling and Potentially Irreversible Serious Adverse Reactions Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and Central Nervous System Effects

Fluoroquinolones, including MAROXI, have been 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 MAROXI. Patients of any age or without pre-existing risk factors have experienced these adverse reactions [see Warnings and Precautions].

Discontinue MAROXI immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including MAROXI, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.

6.2 Tendinitis and Tendon Rupture

Fluoroquinolones, including MAROXI, have been associated with an increased risk of tendinitis and tendon rupture in all ages [see Warnings and Precautions and Adverse Reactions]. This adverse reaction most frequently involves the Achilles tendon, and has also been reported 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. Tendinitis and tendon rupture can occur bilaterally.

The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is increased in patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Other factors that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendinitis and tendon rupture have also occurred in patients taking fluoroquinolones who do not have the above risk factors. Discontinue MAROXI 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 MAROXI, in patients who have a history of tendon disorders or who have experienced tendinitis or tendon rupture [see Adverse Reactions].

Fluoroquinolones, including MAROXI, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving fluoroquinolones including MAROXI. Symptoms may occur soon after initiation of MAROXI and may be irreversible in some patients [see Warnings and Precautions and Adverse Reactions].

Discontinue MAROXI immediately if the patient experiences symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation. Avoid fluoroquinolones, including MAROXI, in patients who have previously experienced peripheral neuropathy

6.3 Central Nervous System Effects

Fluoroquinolones, including MAROXI, have been 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. These adverse reactions may occur following the first dose. If these reactions occur in patients receiving MAROXI, discontinue MAROXI immediately and institute appropriate measures. As with all fluoroquinolones, use MAROXI when the benefits of treatment exceed the risks in patients with known or suspected CNS disorders (for example, severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold [see Drug Interactions].

6.4 Exacerbation of Myasthenia Gravis

Fluoroquinolones, including MAROXI, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Avoid MAROXI in patients with known history of myasthenia gravis.

6.5 Other Serious and Sometimes Fatal Adverse Reactions

Other serious and sometimes fatal adverse reactions, some due to hypersensitivity, and some due to uncertain etiology, have been reported in patients receiving therapy with fluoroquinolones, including MAROXI. These reactions may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

- Fever, rash, or severe dermatologic reactions (for example, toxic epidermal necrolysis, Stevens-Johnson syndrome)
- Vasculitis; arthralgia; myalgia; serum sickness
- Allergic pneumonitis
- Interstitial nephritis; acute renal insufficiency or failure
- Hepatitis; jaundice; acute hepatic necrosis or failure
- Anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities.

Discontinue MAROXI immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and institute supportive measures.

6.6 Hypersensitivity Reactions

Serious anaphylactic reactions, some following the first dose, have been reported in patients receiving fluoroquinolone therapy, including MAROXI. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Discontinue MAROXI at the first appearance of a skin rash or any other sign of hypersensitivity [see Warnings and Precautions].

6.7 *Clostridium difficile*-Associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including MAROXI, 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.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

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.

6.8 Blood Glucose Disturbances

As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycemia and hyperglycemia have been reported with MAROXI. In MAROXI-treated patients, dysglycemia occurred predominantly in elderly diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (for example, sulfonylurea) or with insulin. In diabetic patients, careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs, MAROXI should be discontinued and appropriate therapy should be initiated immediately [see Drug Interactions].

6.9 Photosensitivity/Phototoxicity

Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (for example, burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, "V" area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of fluoroquinolones, including MAROXI, after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. MAROXI should be discontinued if phototoxicity occurs [see Clinical Pharmacology].

6.10 Development of Drug Resistant Bacteria

Prescribing MAROXI 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.

7 ADVERSE REACTIONS

The following serious and otherwise important adverse reactions are discussed in greater detail in the warnings and precautions section of the label:

- Disabling and Potentially Irreversible Serious Adverse Reactions Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and Central Nervous System Effects [see Warnings and Precautions]
- Tendinitis and Tendon Rupture[see Warnings and Precautions]
- Peripheral Neuropathy [see Warnings and Precautions]
- Central Nervous System Effects [see Warnings and Precautions]
- Exacerbation of Myasthenia Gravis [see Warnings and Precautions]
- QT Prolongation [see Warnings and Precautions]
- Other Serious and Sometimes Fatal Adverse Reactions [see Warnings and Precautions]
- Hypersensitivity Reactions [see Warnings and Precautions]
- Clostridium difficile-Associated Diarrhea [see Warnings and Precautions]
- Blood Glucose Disturbances [see Warnings and Precautions]

- Photosensitivity/Phototoxicity [see Warnings and Precautions]
- Development of Drug Resistant Bacteria [see Warnings and Precautions]

7.1 Postmarketing Experience

Table 4 below lists adverse reactions that have been identified during post-approval use of MAROXI. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Table 4: Postmarketing Reports of Adverse Drug Reactions

System Organ Class	Adverse Reactions
Blood and Lymphatic System Disorders	Agranulocytosis Pancytopenia [see Warnings and Precautions
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 [see Warnings and Precautions
Immune System Disorders	Anaphylactic reaction Anaphylactic shock Angioedema (including laryngeal edema) [see Warnings and Precautions (5.7, 5.8)]
Musculoskeletal and Connective Tissue Disorders	Tendon rupture [see Warnings and Precautions (5.2)]
Nervous System Disorders	Altered coordination Abnormal gait [see Warnings and Precautions (5.3)] Myasthenia gravis (exacerbation of) [see Warnings and Precautions (5.5)] Muscle weakness Peripheral neuropathy (that may be irreversible), polyneuropathy [see Warnings and Precautions (5.3)]
Psychiatric Disorders	Psychotic reaction (very rarely culminating in self-injurious behavior, such as suicidal ideation/thoughts or suicide attempts [see Warnings and Precautions (5.4)]
Renal and Urinary Disorders	Interstitial nephritis [see Warnings and Precautions (5.7)]
Respiratory, Thoracic and Mediastinal Disorders	Allergic pneumonitis [see Warnings and Precautions (5.7)]
Skin and Subcutaneous Tissue Disorders	Photosensitivity/phototoxicity reaction [see Warnings and Precautions (5.12)] Stevens-Johnson syndrome Toxic epidermal necrolysis [see Warnings and Precautions (5.7)]

8 DRUG INTERACTIONS

8.1 Antacids, Sucralfate, Multivitamins and other Products Containing Multivalent Cations.

Fluoroquinolones, including MAROXI, form chelates with alkaline earth and transition metal cations. Oral administration of MAROXI with antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, or with formulations containing divalent and trivalent cations such as didanosine buffered tablets for oral suspension or the pediatric powder for oral solution, may substantially interfere with the absorption of MAROXI, resulting in systemic concentrations considerably lower than desired. Therefore, MAROXI should be taken at least 4 hours before or 8 hours after these agents [see Dosage and Administration (2.2) and Clinical Pharmacology].

8.2 Warfarin

Fluoroquinolones, including MAROXI, have been reported 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. Therefore the prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored if MAROXI is administered concomitantly with warfarin or its derivatives [see Adverse Reactions and Clinical Pharmacology].

8.3 Antidiabetic Agents

Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with fluoroquinolones, including MAROXI, and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered. If a hypoglycemic reaction occurs, MAROXI should be discontinued and appropriate therapy should be initiated immediately [see Warnings and Precautions and Adverse Reactions].

8.4 Nonsteroidal Anti-Inflammatory Drugs

The concomitant administration of a nonsteroidal anti-inflammatory drug (NSAID) with a fluoroquinolone, including MAROXI, may increase the risks of CNS stimulation and convulsions [see Warnings and Precautions].

9 USE IN SPECIFIC POPULATIONS

9.1 Pregnancy

Pregnancy Category C. Because no adequate or well-controlled studies have been conducted in pregnant women, MAROXI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day or 0.24 times the maximum recommended human dose based on systemic exposure (AUC), but decreased fetal body weights and slightly delayed fetal skeletal development (indicative of fetotoxicity) were observed. There was no evidence of teratogenicity when pregnant cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (2.5 times the maximum recommended human dose based upon systemic exposure). An increased incidence of smaller fetuses was observed at 100 mg/kg/day. In an oral pre- and postnatal development study conducted in rats, effects observed at 500 mg/kg/day included slight increases in duration of pregnancy and prenatal loss, reduced pup birth weight and decreased neonatal survival. Treatment-related maternal mortality occurred during gestation at 500 mg/kg/day in this study.

9.2 Nursing Mothers

Moxifloxacin is excreted in the breast milk of rats. Moxifloxacin may also be excreted in human milk. Because of the potential for serious adverse reactions in infants who are nursing from mothers taking MAROXI, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

9.3 Pediatric Use

Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. [see Boxed Warning, Warnings and Precautions and Clinical Pharmacology].

9.4 Geriatric Use

Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone such as MAROXI. This risk is further increased in patients receiving concomitant corticosteroid therapy. Tendinitis or tendon rupture can involve the Achilles, hand, shoulder, or other tendon sites and can occur during or after completion of therapy; cases occurring up to several months after fluoroquinolone treatment have been reported. Caution should be used when prescribing MAROXI to elderly patients especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue MAROXI and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur [see Boxed Warning, and Warnings and Precautions].

In controlled multiple-dose clinical trials, 23% of patients receiving oral MAROXI were greater than or equal to 65 years of age and 9% were greater than or equal to 75 years of age. The clinical trial data demonstrate that there is no difference in the safety and efficacy of oral MAROXI in patients aged 65 or older compared to younger adults.

9.5 Renal Impairment

The pharmacokinetic parameters of moxifloxacin are not significantly altered in mild, moderate, severe, or end-stage renal disease. No dosage adjustment is necessary in patients with renal impairment, including those patients requiring hemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD) [see Dosage and Administration (2), and Clinical Pharmacology].

9.6 Hepatic Impairment

No dosage adjustment is recommended for mild, moderate, or severe hepatic insufficiency (Child-Pugh Classes A, B, or C). However, due to metabolic disturbances associated with hepatic insufficiency, which may lead to QT prolongation, MAROXI should be used with caution in these patients [see Warnings and Precaution (5.6) and Clinical Pharmacology].

10 OVERDOSAGE

Single oral overdoses up to 2.8 g were not 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.

10.1 MAROXI Tablets

- MAROXI Tablets are available as film-coated tablets containing moxifloxacin hydrochloride (equivalent to 400 mg moxifloxacin).

10.2 Microbiology

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.

Mechanism of Resistance
The mechanism of action for fluoroquinolones, including moxifloxacin, is different from that of macrolides, beta-lactams, aminoglycosides, or tetracyclines; therefore, microorganisms resistant to these classes of drugs may be susceptible to moxifloxacin. Resistance to fluoroquinolones occurs primarily by a mutation in topoisomerase II (DNA gyrase) or topoisomerase IV genes, decreased outer membrane permeability or drug efflux. In vitro resistance to moxifloxacin develops slowly via multiple-step mutations. Resistance to moxifloxacin occurs in vitro at a general frequency of between 1.8 x 10–9 to < 1 x 10–11 for Gram-positive bacteria.

Cross Resistance
Cross-resistance has been observed between moxifloxacin and other fluoroquinolones against Gram-negative bacteria. Gram-positive bacteria resistant to other fluoroquinolones may, however, still be susceptible to moxifloxacin. There is no known cross-resistance between moxifloxacin and other classes of antimicrobials.

Moxifloxacin has been shown to be active against most isolates of the following bacteria, both in vitro and in clinical infections [see Indications and Usage (1)].

Gram-positive bacteria
Enterococcus faecalis
Staphylococcus aureus
Streptococcus anginosus
Streptococcus constellatus
Streptococcus pneumoniae (including multi-drug resistant isolates [MDRSP] **)
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 pneumoniae
Moraxella catarrhalis
Proteus mirabilis
Yersinia pestis
Anaerobic bacteria
Bacteroides fragilis
Bacteroides thetaiotaomicron
Clostridium perfringens
Peptostreptococcus species
Other microorganisms
Chlamydophila pneumoniae
Mycoplasma pneumoniae

The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for moxifloxacin. However, the efficacy of MAROXI in treating clinical infections due to these bacteria has not been established in adequate and well controlled clinical trials.

Gram-positive bacteria
Staphylococcus epidermidis
Streptococcus agalactiae
Streptococcus viridans group
Gram-negative bacteria
Citrobacter freundii
Klebsiella oxytoca
Legionella pneumophila
Anaerobic bacteria
Fusobacterium species
Prevotella species
Susceptibility Tests Methods

When available, the clinical microbiology laboratory should provide the results of in vitro susceptibility test results for antimicrobial drug products used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Dilution Techniques
Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method (broth and/or agar). 1,2,4 The MIC values should be interpreted according to the criteria in Table 8.

Diffusion Techniques
Quantitative methods that require measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size prove should be determined using a standardized test method.2,3 This procedure uses paper disks impregnated with 5 mcg moxifloxacin to test the susceptibility of bacteria to moxifloxacin. The disc diffusion interpretive criteria are provided in Table 8.

Anaerobic Techniques
For anaerobic bacteria, the susceptibility to moxifloxacin can be determined by a standardized test method.2,5

A report of "Susceptible" indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations at the infection site necessary to inhibit growth of the pathogen. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where a high dosage of the drug product can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations usually achievable at the infection site; other therapy should be selected.

Quality Control
Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay and the techniques of the individuals performing the test.1,2,3,4,5 Standard moxifloxacin powder should provide the following range of MIC values noted in Table 9. For the diffusion technique using the 5 mcg moxifloxacin disk,.

11 HOW SUPPLIED/STORAGE AND HANDLING

Maroxi Tablet
Maroxi 400 mg film coated tablets:
Alu. Alu. Blister pack of 5's tablets.

STORAGE CONDITIONS:
Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F) [see USP Controlled Room Temperature]. Avoid high humidity.

12 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide)

Serious Adverse Reactions
Advise patients to stop taking MAROXI if they experience an adverse reaction and to call their healthcare provider for advice on completing the full course of treatment with another antibacterial drug.
Inform patients of the following serious adverse reactions that have been associated with MAROXI or other fluoroquinolone use:

- **Disabling and potentially irreversible serious adverse reactions that may occur together:** Inform patients that disabling and potentially irreversible serious adverse reactions, including tendinitis and tendon rupture, peripheral neuropathies, and central nervous system effects, have been associated with use of MAROXI and may occur together in the same patient. Inform patients to stop taking MAROXI immediately if they experience an adverse reaction and to call their healthcare provider.
- **Tendinitis and Tendon Rupture:** Instruct patients to contact their healthcare provider if they experience pain, swelling, or inflammation of a tendon, or weakness or inability to use one of their joints; rest and refrain from exercise; and discontinue MAROXI treatment. Symptoms may be irreversible. The risk of severe tendon disorder with fluoroquinolones is higher in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.
- **Peripheral Neuropathies:** Inform patients that peripheral neuropathies have been associated with MAROXI use, symptoms may occur soon after initiation of therapy and may be irreversible. If symptoms of peripheral neuropathy including pain, burning, tingling, numbness and/or weakness develop, immediately discontinue MAROXI and tell them to contact their physician.
- **Central nervous system effects** (for example, convulsions, dizziness, lightheadedness, increased intracranial pressure): Inform patients that convulsions have been reported in patients receiving fluoroquinolones, including MAROXI. Instruct patients to notify their physician before taking this drug if they have a history of convulsions. Inform patients that they should know how they react to MAROXI before they operate an automobile or machinery or engage in other activities requiring mental alertness and coordination. Instruct patients to notify their physician if persistent headache with or without blurred vision occurs.
- **Exacerbation of Myasthenia Gravis:** Instruct patients to inform their physician of any history of myasthenia gravis. Instruct patients to notify their physician if they experience any symptoms of muscle weakness, including respiratory difficulties.

- **Hypersensitivity Reactions:** Inform patients that MAROXI can cause hypersensitivity reactions, even following a single dose, and to discontinue the drug at the first sign of a skin rash, hives or other skin reactions, a rapid heartbeat, difficulty in swallowing or breathing, any swelling suggesting angioedema (for example, swelling of the lips, tongue, face, tightness of the throat, hoarseness), or other symptoms of an allergic reaction.
- **Hepatotoxicity:** Inform patients that severe hepatotoxicity (including acute hepatitis and fatal events) has been reported in patients taking MAROXI. Instruct patients to inform their physician if they experience any signs or symptoms of liver injury including: loss of appetite, nausea, vomiting, fever, weakness, tiredness, right upper quadrant tenderness, itching, yellowing of the skin and eyes, light colored bowel movements or dark colored urine.
- **Diarrhea:** Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, instruct patients to contact their physician as soon as possible.
- **Prolongation of the QT Interval:** Instruct patients to inform their physician of any personal or family history of QT prolongation or proarrhythmic conditions such as hypokalemia, bradycardia, or recent myocardial ischemia; if they are taking any Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents. Instruct patients to notify their physician if they have any symptoms of prolongation of the QT interval, including prolonged heart palpitations or a loss of consciousness.
- **Photosensitivity/Phototoxicity:** Inform patients that photosensitivity/phototoxicity has been reported in patients receiving fluoroquinolones. Inform patients to minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while taking quinolones. If patients need to be outdoors while using quinolones, instruct them to wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. If a sunburn-like reaction or skin eruption occurs, instruct patients to contact their physician.
- **Blood Glucose Disturbances:** Inform the patients that if they are diabetic and are being treated with insulin or an oral hypoglycemic agent and a hypoglycemic reaction occurs, they should discontinue MAROXI and consult a physician.

ماروکسی ٹیبلیٹس

(موکسی فلاکساسن)

۴۰۰ ملی گرام ٹیبلیٹس

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: صرف مستند ڈاکٹر کے نسخہ پر فروخت کی جائے۔

۳۰ ڈگری سے کم درجہ حرارت رکھیں۔ دھوپ اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

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