MOXIFLOXACIN HYDROCHLORIDE - moxifloxacin hydrochloride tablet
TORRENT PHARMACEUTICALS LIMITED

WARNINGS AND PRECAUTIONS

CONTRAINDICATIONS

Moxifloxacin hydrochloride tablets are contraindicated in patients with known hypersensitivity to moxifloxacin or other quinolones (4, 5.8) and other antibacterial drugs. Moxifloxacin hydrochloride tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. (1.8)

The following information should be considered when selecting or changing antibacterial therapy:

1. Acute bacterial exacerbation of chronic bronchitis (1.7)
2. Acute bacterial sinusitis (1.6)
3. Skin and Skin Structure Infections: Uncomplicated (1.2) and Complicated (1.3)
4. Complicated intra-abdominal infections (1.4)
5. Plague (1.5)

Indications and Usage, Acute bacterial Sinusitis (1.6)                                                   7/2016
Indications and Usage, Acute Bacterial Exacerbation of chronic Bronchitis (1.7)                           7/2016
Dosage and Administration, Dosage in Adult Patients  (2.1)                         7/2016

Recent Major Changes

Type of Infection   Dose   Duration (days)
Community Acquired Pneumonia (1.1)  400 mg   5 to 14
Uncomplicated Skin and Skin Structure Infections (SSSI) (1.2)  400 mg   7 to 14
Complicated SSSI (1.3)  400 mg   7 to 21
Complicated intra-abdominal Infections (1.4)  400 mg   5 to 14
Plague (1.5)  400 mg   10 to 14
Acute Bacterial Sinusitis (1.6)  400 mg   10 to 14
Acute Bacterial Exacerbation of Chronic Bronchitis (1.7)  400 mg   5

DOSAGE AND ADMINISTRATION

Moxifloxacin hydrochloride tablets, for oral use

1. Acute bacterial exacerbation of chronic bronchitis (1.7)
   - No dosage adjustment in patients with renal or hepatic impairment. (8.6, 8.7)

2. Acute Bacterial Sinusitis (1.6)
   - If infection is due to susceptible strains of the following organisms: Haemophilus influenzae, Moraxella catarrhalis, Staph. aureus (including MRSA), Streptococcus pneumoniae.

3. Skin and Skin Structure Infections: Uncomplicated (1.2)
   - If infection is caused by susceptible strains of the following organisms: Staph. aureus (including MRSA), Staph. epidermidis, Micrococcus, Propionibacterium acnes, Pseudomonas aeruginosa, Staph. aureus (including MRSA), Streptococcus pyogenes, Streptococcus agalactiae, and S. aureus, including methicillin-resistant S. aureus (MRSA).

4. Complicated SSSI (1.3)
   - If infection is caused by susceptible strains of the following organisms: Staph. aureus (including MRSA), Staph. epidermidis, Propionibacterium acnes, Staph. aureus (including MRSA), Staph. epidermidis, Propionibacterium acnes, and Streptococcus pyogenes.

5. Complicated intra-abdominal infections (1.4)
6. Plague (1.5)

Dosage and Administration, Dosage in Adult Patients  (2.1)                         7/2016

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

Recent Major Changes

Full Prescribing Information: Contents

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

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800-FDA-1088 or www.fda.gov/medwatch

To report SUSPECTED ADVERSE REACTIONS, contact Torrent Pharma Inc. at 1-269-544-2299

Rx Only

MOXIFLOXACIN HYDROCHLORIDE tablets, for oral use

TABLETS.

These highlights do not include all the information needed to use MOXIFLOXACIN HYDROCHLORIDE safely and effectively. See full prescribing information for MOXIFLOXACIN HYDROCHLORIDE TABLETS.

WARNINGS AND PRECAUTIONS

See full prescribing information for complete boxed warning

- Fluoroquinolones, including moxifloxacin hydrochloride, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together (5.5) including:
  - Tendinitis and tendon rupture (5.2)
  - Peripheral Neuropathy (5.3)
  - Central nervous system effects (5.4)

Discontinue moxifloxacin hydrochloride immediately and avoid the use of fluoroquinolones, including moxifloxacin hydrochloride, if patients experience any of these serious adverse reactions (5.2).

- Fluoroquinolones, including moxifloxacin hydrochloride, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid moxifloxacin hydrochloride in patients with known history of myasthenia gravis (5.5). Because fluoroquinolones, including moxifloxacin hydrochloride, have been associated with serious adverse reactions (5.2 to 5.5), reserve moxifloxacin hydrochloride for use in patients who have no alternative treatment options for the following indications:
  - Acute bacterial sinusitis (1.6)
  - Acute bacterial exacerbation of chronic bronchitis (1.7)

800-FDA-1088 or www.fda.gov/medwatch

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FULL PRESCRIBING INFORMATION

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

- Fluoroquinolones, including moxifloxacin hydrochloride, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together (5.1) including:
  - Tendinitis and tendon rupture [see Warnings and Precautions (5.2)]
  - Peripheral Neuropathy [see Warnings and Precautions (5.3)]
  - Central nervous system effects [see Warnings and Precautions (5.4)]

Discontinue moxifloxacin hydrochloride immediately and avoid the use of fluoroquinolones, including moxifloxacin hydrochloride, in patients who experience any of these serious adverse reactions [see Warnings and Precautions (5.1)]

- Fluoroquinolones, including moxifloxacin hydrochloride, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid moxifloxacin hydrochloride in patients with known history of myasthenia gravis [see Warnings and Precautions (5.5)].

Because fluoroquinolones, including moxifloxacin hydrochloride, have been associated with serious adverse reactions [see Warnings and Precautions (5.1)] and rarely, severe exacerbations of myasthenia gravis, and peripheral neuropathy (including multi-drug resistant Staphylococcus pneumoniae [MDRSP]), Homopneumonia influenzae, Moraxella catarrhalis, methicillin-resistant Staphylococcus aureus, Klebsiella pneumoniae, Mycoplasma pneumoniae, or Chlamydiophila pneumoniae [see Clinical Studies (14.3)].

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

1 INDICATIONS AND USAGE
1.1 Community Acquired Pneumonia

Moxifloxacin hydrochloride tablets are indicated in adult patients for the treatment of Community Acquired Pneumonia caused by susceptible isolates of Streptococcus pneumoniae (including multi-drug resistant Staphylococcus pneumoniae [MDRSP]), Homopneumonia influenzae, Moraxella catarrhalis, methicillin-resistant Staphylococcus aureus, Klebsiella pneumoniae, Mycoplasma pneumoniae, or Chlamydiophila pneumoniae [see Clinical Studies (14.3)].

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

1.2 Uncomplicated Skin and Skin Structure Infections

Moxifloxacin hydrochloride tablets are 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 (14.4)].

1.3 Complicated Skin and Skin Structure Infections

Moxifloxacin hydrochloride tablets are 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 (14.5)].

1.4 Complicated intra-Abdominal Infections

Moxifloxacin hydrochloride tablets are indicated in adult patients for the treatment of Complicated intra-Abdominal Infections (cIAI) 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 (14.6)].
Moxifloxacin hydrochloride tablets are indicated in adult patients for the treatment of plague, including pneumonic and septemic plague, due to susceptible isolates of Yersinia pestis and prophylaxis of plague in adult patients. Efficacy studies of moxifloxacin could not be conducted in humans with plague for feasibility reasons. Therefore this indication is based on an efficacy study conducted in animals only [see Clinical Studies (14.7)].

1.5 Plague
Moxifloxacin hydrochloride tablets are 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 (14.1)].

Because fluoroquinolones, including moxifloxacin hydrochloride, have been associated with serious adverse reactions (see Warnings and Precautions (5.1 and 5.3)) and for some patients ABS is self-limiting, reserve moxifloxacin hydrochloride for treatment of ABS in patients who have no alternative treatment options.

1.6 Acute Bacterial Sinusitis
Moxifloxacin hydrochloride tablets are indicated in adult patients for the treatment of Acute Bacterial Sinusitis (ABS) caused by susceptible isolates of Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis [see Clinical Studies (14.1)].

Because fluoroquinolones, including moxifloxacin hydrochloride, have been associated with serious adverse reactions (see Warnings and Precautions (5.1 and 5.3)) and for some patients ABS is self-limiting, reserve moxifloxacin hydrochloride for treatment of ABS in patients who have no alternative treatment options.

1.7 Acute Bacterial Exacerbation of Chronic Bronchitis
Moxifloxacin hydrochloride tablets are 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 (14.2)].

Because fluoroquinolones, including moxifloxacin hydrochloride, have been associated with serious adverse reactions (see Warnings and Precautions (5.1 and 5.3)) and for some patients ABECB is self-limiting, reserve moxifloxacin hydrochloride for treatment of ABECB in patients who have no alternative treatment options.

1.8 Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of moxifloxacin hydrochloride tablets and other antibacterial drugs, moxifloxacin hydrochloride tablets 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.

2 DOSAGE AND ADMINISTRATION
2.1 Dosage in Adult Patients
The dose of moxifloxacin is 400 mg (orally) once every 24 hours. The duration of therapy depends on the type of infection as described in Table 1.

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Dose Every 24 Hours</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Acquired Pneumonia (1.1)</td>
<td>400 mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Uncomplicated Skin and Soft Tissue Infections (SSSI) (1.2)</td>
<td>400 mg</td>
<td>7</td>
</tr>
<tr>
<td>Complicated SSSI (1.3)</td>
<td>400 mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Complicated Intra-Abdominal Infection (1.4)</td>
<td>400 mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Plague (1.5)</td>
<td>400 mg</td>
<td>7 to 14</td>
</tr>
<tr>
<td>Acute Bacterial Sinusitis (ABS) (1.6)</td>
<td>400 mg</td>
<td>10</td>
</tr>
<tr>
<td>Acute Bacterial Exacerbation of Chronic Bronchitis (ABECB) (1.7)</td>
<td>400 mg</td>
<td>5</td>
</tr>
</tbody>
</table>

a) Due to the designated pathogens [see Indications and Usage (1)].

b) Sequential therapy (intravenous to oral) may be continued as the discretion of the physician.

c) Drug administration should begin as soon as possible after suspected or confirmed exposure to Yersinia pestis.

Conversion of Intravenous to Oral Dosing in Adults
Intravenous formulation is indicated when it offers a route of administration advantageous to the patient (for example, patient cannot tolerate an oral dosage form). When switching from intravenous to oral formulation, no dosage adjustment is necessary. Patients whose therapy is started with moxifloxacin hydrochloride injection may be switched to moxifloxacin hydrochloride tablets when clinically indicated at the discretion of the physician.

2.3 Important Administration Instructions
Moxifloxacin Hydrochloride Tablets

With Multivalent Cations
Administer moxifloxacin hydrochloride tablets at least 4 hours before or 8 hours after products containing magnesium, aluminum, iron or zinc, including amlopidine, sacub barring, multivitamins and didanosine buffered tablets for oral suspension or the pediatric powder for oral solution [see Drug Interactions (7.1) and Clinical Pharmacology (12.3)].

With Food
Moxifloxacin hydrochloride tablets can be taken with or without food, drink fluids liberally.

3 DOSAGE FORMS AND STRENGTHS
3.1 Moxifloxacin Hydrochloride Tablets
Light pink colored, capsule shaped, biconvex, film-coated tablets debossed with ‘1201’ on one side and ‘400’ on other containing moxifloxacin hydrochloride (equivalent to 400 mg moxifloxacin).

4 CONTRAINDICATIONS
Moxifloxacin hydrochloride tablets are contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antibacterials [see Warnings and Precautions (5.8)].

5 WARNINGS AND PRECAUTIONS
5.1 Disabling and Potentially Irreversible Serious Adverse Reactions Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and Central Nervous System Effects
Fluoroquinolones, including moxifloxacin hydrochloride, 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, arthritis, 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 hydrochloride. Patients of any age or without pre-existing risk factors have experienced these adverse reactions [see Warnings and Precautions (5.2, 5.3, 5.4)].

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

5.2 Tendinitis and Tendon Rupture
Fluoroquinolones, including moxifloxacin hydrochloride, have been associated with an increased risk of tendinitis and tendon rupture in all ages [see Warnings and Precautions (5.1) and Adverse Reactions (6.2)]. 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 usually 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 moxifloxacin hydrochloride immediately if the patient experiences posterior subtended inflammation or rupture of a tendon. Patients should be advised to stop 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 hydrochloride tablets, in patients who have a history of tendon disorders or who have experienced tendinitis or tendon rupture [see Adverse Reactions (6.2)].

5.3 Peripheral Neuropathy
Fluoroquinolones, including moxifloxacin hydrochloride, 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, hypoesthesia, dysesthesias and weakness have been reported in patients receiving fluoroquinolones including moxifloxacin hydrochloride tablets. Symptoms may occur soon after initiation of moxifloxacin hydrochloride tablets and may be irreversible in some patients [see Warnings and Precautions (5.1) and Adverse Reactions (6.1, 6.2)].

Discontinue moxifloxacin hydrochloride 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 moxifloxacin hydrochloride, in patients who have previously experienced peripheral neuropathy.

5.4 Central Nervous System Effects
Fluoroquinolones, including moxifloxacin hydrochloride, have been associated with an increased risk of central nervous system (CNS) reactions, including: convolution and increased intracranial pressure (including pseudotumor cerebri) and toxic psychosis. Fluoroquinolones may also cause CNS reactions of nervousness, agitation, insomnia, anxiety, nightmares, paraesthesia, 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 moxifloxacin hydrochloride tablets, discontinue moxifloxacin hydrochloride immediately and institute appropriate measures. As with all fluoroquinolones, use moxifloxacin hydrochloride tablets when the benefit of treatment exceeds 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 (7.4)].

5.5 Exacerbation of Myasthenia Gravis
Fluoroquinolones, including moxifloxacin hydrochloride, 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 moxifloxacin hydrochloride in patients with a history of myasthenia gravis.

5.6 QT Prolongation
Moxifloxacin hydrochloride has been shown to prolong the QT interval of the electrocardiogram in some patients. Following oral dosing with 400 mg of moxifloxacin the mean (± SD) change in QTc from the pre-dose value at the time of maximum drug concentration was 6 msec (± 20) (n = 787). Following a course of daily intravenous dosing (400 mg; 1 hour infusion each day) the mean change in QTc from the Day 1 pre-dose value was 19 msec (± 22) on Day 1 (n = 687) and 7 msec (± 24) on Day 3 (n = 667).

Avoid moxifloxacin hydrochloride 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

Elderly patients using intravenous moxifloxacin hydrochloride may be more susceptible to drug-associated QT prolongation. [See Use In Specific Populations (8.5)]

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 hydrochloride. [See Clinical Pharmacology (12.3)].

The magnitude of QT prolongation may increase with increasing concentrations of the drug or increasing rates of infusion of the intravenous formulation. Therefore the recommended dose or infusion rate should not be exceeded.

In premarketing clinical trials, the rate of cardiovascular adverse reactions was similar in 798 moxifloxacin hydrochloride and 702 comparator treated patients who received concomitant therapy with non-quinolone antimicrobial drugs. The incidence of ECG abnormalities including abnormal QTc or QT interval 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 was low. [See Clinical Pharmacology (12.2)].

5.7 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 fluoroquinolones including moxifloxacin hydrochloride, including:
- Fever, rash, or severe dermatologic reactions (for example, toxic epidermal necrolysis, Stevens-Johnson syndrome)
- Vascular: arteritis; myalgia; sepsis
- Allergic pneumonitis
- Intestinal: cholestasis
- Allergic: hypersensitivity
- Nerve: 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 moxifloxacin hydrochloride, in patients who have previously experienced peripheral neuropathy.
- Other serious and sometimes fatal adverse reactions, some due to hypersensitivity, and some due to uncertain etiology, have been reported in patients receiving fluoroquinolones including moxifloxacin hydrochloride, including:
- Arthralgia; myalgia; serum sickness
- Vascular: angioedema, angioneurotic edema, hypotension, syncope
- Nerve: optic neuropathy; optic neuritis; retinal vasculitis; thiamine deficiency; retinopathy; papilledema
- Other: hypoglycemia, neutropenia, anemia, agranulocytosis, thrombocytopenia

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

5.8 Hypersensitivity Reactions
Serious anaphylactic reactions, some following the first dose, have been reported in patients receiving fluoroquinolone therapy, including moxifloxacin hydrochloride. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Discontinue moxifloxacin hydrochloride as the first appearance of a skin rash or any other sign of hypersensitivity. [See Warnings and Precautions (5.7)].

5.9 Clostridium difficile-Associated Diarrhea
Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, especially fluoroquinolones, and may range from mild to severe. Hypertonic saline enemas are the preferred treatment for mild to moderate CDAD. For severe, extensive, or fulminant infections where CDAD is a life-threatening complication, vancomycin or metronidazole is recommended. [see Warnings and Precautions (5.9)].
agons, including moxifloxacin hydrochloride, 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. Hypertoxinemia producing strain 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 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.

5.10 Arthropathic Effects in Animals

In immature dogs, oral administration of moxifloxacin hydrochloride caused lameness. Histopathological examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage. Related quinolone-class drugs also produce erosion of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species. [See Nonclinical Toxicology (13.2)].

5.11 Blood Glucose Disturbances

As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycemia and hyperglycemia have been reported with moxifloxacin hydrochloride. In moxifloxacin hydrochloride-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, moxifloxacin hydrochloride should be discontinued and appropriate therapy should be initiated immediately. [See Drug Interactions (7.3)].

5.12 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 moxifloxacin hydrochloride, after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Moxifloxacin hydrochloride should be discontinued if phototoxicity occurs. [See Clinical Pharmacology (12.2)].

5.13 Development of Drug Resistant Bacteria

Prescribing moxifloxacin hydrochloride 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.

6 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 (5.1)].
- Tendinitis and Tendon Rupture [see Warnings and Precautions (5.2)].
- Peripheral Neuropathy [see Warnings and Precautions (5.3)].
- Central Nervous System Effects [see Warnings and Precautions (5.4)].
- Exacerbation of Myasthenia Gravis [see Warnings and Precautions (5.5)].
- QT Prolongation [see Warnings and Precautions (5.6)].
- Other Serious and Sometimes Fatal Adverse Reactions [see Warnings and Precautions (5.7)].
- Hypersensitivity Reactions [see Warnings and Precautions (5.8)].
- Clostridium difficile-Associated Diarrhea [see Warnings and Precautions (5.9)].
- Blood Glucose Disturbances [see Warnings and Precautions (5.10)].
- Photosensitivity/Phototoxicity [see Warnings and Precautions (5.11)].
- Development of Drug Resistant Bacteria [see Warnings and Precautions (5.13)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to moxifloxacin hydrochloride in 14,981 patients in 71 active controlled Phase II/IV clinical trials in different indications [see Indications and Usage (1)]. The population studied had a mean age of 50 years (approximately 73% of the population was less than 65 years of age), 50% were male, 63% were Caucasian, 12% were Asian, and 9% were Black. Patients received moxifloxacin 400 mg once daily oral, intravenous, or sequentially (intravenous followed by oral). Treatment duration was usually 6 to 10 days, and the mean number of days on therapy was 9 days.

Discontinuation of moxifloxacin due to adverse reactions occurred in 5% of patients overall, 4% of patients treated with 400 mg PO, 4% with 400 mg intravenous and 8% with sequential therapy (400 mg PO, 400 mg intravenous). The most common adverse reactions leading to discontinuation with the 400 mg intravenous dose was rash. The most common adverse reactions leading to discontinuation with the 400 mg intravenous or sequential dose were diarrhea, pyrexia, and vomiting. Adverse reactions occurring in 1% of moxifloxacin hydrochloride-treated patients and less common adverse reactions, occurring in 0.1 to 1% of moxifloxacin hydrochloride-treated patients, are shown in Tables 2 and 3, respectively. The most common adverse drug reactions (3%) are nausea, diarrhea, headache, and dizziness.

Table 2: Common (1% or more) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin Hydrochloride

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reactions</th>
<th>% (N=14,981)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Nausea</td>
<td>7</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Diarrhea</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>1</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Pyrexia</td>
<td>1</td>
</tr>
<tr>
<td>Investigations</td>
<td>Alkaline phosphatase increased</td>
<td>4</td>
</tr>
<tr>
<td>Metabolism and Nutritional Disorder</td>
<td>Hypokalemia</td>
<td>1</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Headache</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>3</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>Inomnia</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3: Less Common (0.1 to less than 1%) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin Hydrochloride (N=14,981)

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Tendinopathy</td>
</tr>
<tr>
<td></td>
<td>Eosinophilia</td>
</tr>
<tr>
<td></td>
<td>Neutropenia</td>
</tr>
<tr>
<td></td>
<td>Leukopenia</td>
</tr>
<tr>
<td></td>
<td>Leukocytosis</td>
</tr>
</tbody>
</table>
Cardiac Disorders
- Atrial fibrillation
- Palpitations
- Tachycardia
- Angina pectoris
- Cardiac failure
- Cardiac arrest
- Bradycardia

Ear and Labyrinth Disorders
- Vertigo
- Tinnitus

Eye Disorders
- Vision blurred

Gastrointestinal Disorders
- Dry mouth
- Abdominal discomfort
- Flatulence
- Gastroesophageal reflux disease
- Gastritis

General Disorders and Administration Site Conditions
- Fatigue
- Chest pain
- Anemia
- Infusion site extravasation
- Edema
- Chills
- Chest discomfort
- Facial pain

Hepatobiliary Disorders
- Hepatic function abnormal

Infections and Infestations
- Candidiasis
- Vaginal infection
- Fungal infection
- Gastroenteritis

Investigations
- Aspartate aminotransferase increased
- Gamma-glutamyltransferase increased
- Blood alkaline phosphatase increased
- Electrocardiogram QT prolonged
- Blood lactate dehydrogenase increased
- Blood triglycerides increased

Metabolism and Nutrition Disorders
- Hyperglycemia
- Agranulocytosis
- Neutropenia
- Decreased appetite
- Dehydration

Musculoskeletal and Connective Tissue Disorders
- Back pain
- Pain in extremity
- Arthralgia
- Muscle weakness
- Musculoskeletal pain

Nervous System Disorders
- Dysgeusia
- Somnolence
- Tremor
- Lethargy
- Paresthesia
- Hypoesthesia
- Syncope

Psychiatric Disorders
- Anxiety
- Confusional state
- Agitation
- Depression
- Nervousness
- Restlessness
- Hallucinations

Renal and Urinary Disorders
- Renal failure
- Dysuria

Reproductive System and Breast Disorders
- Vulvovaginal pruritus

Respiratory, Thoracic, and Mediastinal Disorders
- Dyspnea
- Asthma
- Wheezing
- Bronchospasm

Skin and Subcutaneous Tissue Disorders
- Rash
- Pruritus
- Urticaria
- Dermatitis allergic
- Night sweats

Vascular Disorders
- Hypertension
- Hypotension
- Phlebitis

Laboratory Changes
Changes in laboratory parameters, which are not listed above and which occurred in 2% or more of patients and at an incidence greater than in controls included: increases in mean corpuscular hemoglobin (MCH), neutrophils, white blood cells (WBCs), prothrombin time (PT) ratio, ionized calcium, chloride, albumin, globulin, bilirubin decreases in hemoglobin, red blood cells (RBCs), neutrophils, eosinophils, basophils, glucose, oxygen partial pressure (pO2), fibrinogen, and amylase. It cannot be determined if any of the above laboratory abnormalities were caused by the drug or the underlying condition being treated.

6.2 Postmarketing Experience
Table 4 below lists adverse reactions that have been identified during post-approval use of moxifloxacin hydrochloride. 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>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Agranulocytosis</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Ventricular tachyarrhythmias (including in very rare cases cardiac arrest and torsade de pointes, and usually in patients with concurrent severe underlying proarrhythmic conditions)</td>
</tr>
</tbody>
</table>
Animal reproductive and development studies were done in rats, rabbits, and cynomolgus macaques. Moxifloxacin was not teratogenic when administered to pregnant rats (IV and oral), rabbits (IV), and monkeys (oral, exposures that were 0.25-2.5 times those at the human clinical dose (400 mg/day moxifloxacin hydrochloride tablets). However, when moxifloxacin was administered to rats and rabbits during pregnancy and throughout lactation (rat only) at doses associated with maternal toxicity, decreased neonatal body weights, increased incidence of skeletal variations (rib and vertebrae combined), and increased fetal loss were observed (see Data). Advise pregnant women of the potential risk to the fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

**Data**

Animal Data

Animal reproductive and development studies were done in rats, rabbits, and cynomolgus macaques. Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis (gestation days 6 to 17) at oral doses as high as 500 mg/kg/day or 2.4 times the maximum recommended human dose based on systemic exposure (AUC), but decreased fetal body weights and slightly delayed fetal skeletal development were observed. Intravenous administration of 80 mg/kg/day (approximately 2 times the maximum recommended human dose based on body surface area) to pregnant rats resulted in maternal toxicity and a marginal effect on fetal and placental weights and the appearance of the placenta. (Gestation days 6 to 17). There was no evidence of teratogenicity at intravenous doses as high as 80 mg/kg/day (approximately 2 times the maximum recommended human dose based on body surface area) in pregnant rats during organogenesis (gestation days 6 to 17). Intravenous administration of 20 mg/kg/day (approximately equal to the maximum recommended human oral dose based upon systemic exposure) to pregnant rabbits during organogenesis (gestation days 6 to 20) resulted in decreased fetal body weights and delayed fetal skeletal ossification. When rib and vertebral malformations were combined, there was an increased fetal and litter incidence of these effects in rabbits. Sign of maternal toxicity in rabbits at this dose included mortality, abortions, marked reduction of food consumption, decreased water intake, body weight loss and hyperactivity. There was no evidence of teratogenicity when pregnant cynomolgus macaques were given oral doses as high as 100 mg/kg/day (2.5 times the maximum recommended human dose based on body surface area) to pregnant rabbits (oral administration of 100 mg/kg/day) resulted in decreased fetal body weights, increased incidence of skeletal variations (ribs and vertebrae combined), and increased fetal loss were observed (see Data). Advise pregnant women of the potential risk to the fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

**Drug Interactions**

7. Drug Interactions

7.1 Antacids, Sucralfate, Multivitamins and Other Products Containing Multivalent Cations

Fluoroquinolones, including moxifloxacin hydrochloride, 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, or with formulations containing divalent and trivalent cations such as dimenhydrinate tablets for oral suspension or the pediatric powder for oral solution, may substantially interfere with the absorption of moxifloxacin hydrochloride, resulting in systemic concentrations considerably lower than desired. Therefore, moxifloxacin hydrochloride should be taken at least 4 hours before or 8 hours after these agents. [See Dosage and Administration (2.2) and Clinical Pharmacology (12.3)].

7.2 Warfarin

Fluoroquinolones, including moxifloxacin hydrochloride, 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 moxifloxacin is administered concomitantly with warfarin or its derivatives. [See Adverse Reactions (6.2) and Clinical Pharmacology (12.3)].

7.3 Antidiabetic Agents

Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with fluoroquinolones, including moxifloxacin hydrochloride, and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered. If a hypoglycemic reaction occurs, moxifloxacin hydrochloride should be discontinued and appropriate therapy should be initiated immediately. [See Warnings and Precautions (5.11) and Adverse Reactions (6.1)].

7.4 Nonsteroidal Anti-Inflammatory Drugs

The coadministration of a nonsteroidal anti-inflammatory drug (NSAID) with a fluoroquinolone, including moxifloxacin hydrochloride, may increase the risks of CNS stimulation and convulsions [see Warnings and Precautions (5.3)].

7.5 Drugs that Prolong QT

There is limited information available on the potential for a pharmacodynamic interaction in humans between moxifloxacin hydrochloride and other drugs that prolong the QTc interval of the electrocardiogram. Sotalol, a Class III antiarrhythmic, has been shown to further increase the QTc interval when combined with high doses of intravenous moxifloxacin hydrochloride in dogs. Therefore, moxifloxacin hydrochloride should be avoided with Class IA and Class III antiarrhythmics. [See Warnings and Precautions (5.5) and Nonclinical Toxicology (13.2)].
Moxifloxacin is a member of the fluoroquinolone class of antibacterial agents. It is a synthetic antibacterial agent for oral administration. Moxifloxacin, a diazabicyclo[4.3.0]non-8-yl-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinoline carboxylic acid. It is available as moxifloxacin hydrochloride tablets containing moxifloxacin hydrochloride, USP (240 mg) and inactive ingredients which may include colloidal silicon dioxide, croscarmellose sodium, ferric oxide red, hydroxypropyl magnesium sesquisulfate, microcrystalline cellulose, polyethylene glycol 400, polyvinyl pyrrolidone, pregelatinized starch, and titanium dioxide.

12.1 Mechanism of Action
Moxifloxacin is a member of the fluoroquinolone class of antibacterial agents [see Microbiology (2.3)].

12.2 Pharmacodynamics
Phenoxymethyl potential

12.3 Clinical Pharmacology

8.2 Lactation
Risk summary
It is not known if moxifloxacin is present in human milk. Based on animal studies in rats, moxifloxacin may be excreted in human milk. (See Data). The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for moxifloxacin hydrochloride and any potential adverse effects on the breastfeeding infant from moxifloxacin hydrochloride or from the underlying maternal condition.

Data
In lactating rats given a single oral dose of 4.59 mg/kg moxifloxacin (approximately 9 times less than the recommended human dose based on body surface area) 8 days postpartum, there was very low excretion of substrate-related radioactivity into the milk, amounting to approximately 0.03% of the dose.

8.4 Pediatric Use
Effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. Moxifloxacin hydrochloride causes arthropathy in juvenile animals [see Warnings and Precautions (5.10), and Nonclinical Toxicology (13.2)]. Information describing a clinical study in children in which efficacy was not demonstrated in pediatric patients is approved for Bayer Healthcare Pharmaceuticals Inc.'s AVELOX (moxifloxacin hydrochloride). However, due to Bayer Healthcare Pharmaceuticals Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information.

8.5 Geriatric Use
Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone such as moxifloxacin hydrochloride. 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 occur during or after completion of therapy, cases occurring up to several months after fluoroquinolone treatment have been reported.

Cautions should be used when prescribing moxifloxacin hydrochloride to elderly patients especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue moxifloxacin hydrochloride and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur. [See Warnings and Precautions (5.2)].

In controlled multiple-dose clinical trials, 23% of patients receiving oral moxifloxacin hydrochloride 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 moxifloxacin hydrochloride in patients aged 65 or older compared to younger adults.

In trials of intravenous use, 42% of moxifloxacin hydrochloride patients were greater than or equal to 65 years of age and 22% were greater than or equal to 75 years of age. The clinical trial data demonstrate that the safety of intravenous moxifloxacin hydrochloride in patients aged 65 or older was similar to that of comparator-treated patients. In general, elderly patients may be more susceptible to drug-associated effects of the QT interval. Therefore, moxifloxacin should be avoided in patients taking drugs that can result in prolongation of the QT interval (for example, class IA or class III antiarrhythmics) or in patients with risk factors for torsade de points (for example, known QT prolongation, uncorrected hypokalemia). [See Warnings and Precautions (5.6), Drug Interactions (7.5), and Clinical Pharmacology (12.3)].

8.6 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 (12.3)].

8.7 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, moxifloxacin should be used with caution in these patients [see Warnings and Precaution (5.6) and Clinical Pharmacology (12.3)].

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 2% and 4.5% of its glucuronide metabolite are removed by continuous ambulatory peritoneal dialysis and hemodialysis, respectively.

11. DESCRIPTION
Moxifloxacin hydrochloride is a synthetic antibacterial agent for oral administration. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt of 1-cyclopropyl-7-[(5S,8S,8aS)-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 417.9. Its molecular formula is C_{24}H_{22}F_{2}N_{5}O_{5}+HCl and its chemical structure is as follows:

11.1 Moxifloxacin Hydrochloride Tablets

- Moxifloxacin hydrochloride tablets are available as film-coated tablets containing moxifloxacin hydrochloride, USP equivalent to 240 mg moxifloxacin.
- The inactive ingredients are colloidal silicon dioxide, croscarmellose sodium, ferric oxide red, hyprothene, magnesium sesquisulfate, microcrystalline cellulose, polyethylene glycol 400, polyvinyl pyrrolidone, pregelatinised starch and titanium dioxide.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Moxifloxacin is a member of the fluoroquinolone class of antibacterial agents [see Microbiology (2.3)].

12.2 Pharmacodynamics
Phenoxymethyl potential

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12.1 Mechanism of Action
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12.2 Pharmacodynamics
Phenoxymethyl potential

11.1 Moxifloxacin Hydrochloride Tablets

- Moxifloxacin hydrochloride tablets are available as film-coated tablets containing moxifloxacin hydrochloride, USP (240 mg).
- The inactive ingredients are colloidal silicon dioxide, croscarmellose sodium, ferric oxide red, hyprothene, magnesium sesquisulfate, microcrystalline cellulose, polyethylene glycol 400, polyvinyl pyrrolidone, pregelatinised starch and titanium dioxide.
A study of the skin response to ultraviolet (UVA and UVB) and visible radiation conducted in 32 healthy volunteers (8 per group) demonstrated that moxifloxacin does not show phototoxicity in comparison to placebo. The minimum erythematous dose (MED) was measured before and after treatment with moxifloxacin (200 mg or 400 mg once daily), lonefloxacin (400 mg once daily), or placebo. In this study, the MED measured for both doses of moxifloxacin were not significantly different from placebo, while lonefloxacin significantly lowered the MED. (See Warnings and Precautions (5.12)).

13.2 Pharmacokinetics

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).

Moxifloxacin is approximately 30 to 50% bound to serum proteins, independent of drug concentration.

Distribution
Moxifloxacin is well absorbed from the gastrointestinal tract. The absolute bioavailability 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 or intravenous administration of 400 mg. Moxifloxacin concentrations measured post-dose in various tissues and fluids following a 400 mg oral or intravenous dose are summarized in Table 7. The rates of elimination of moxifloxacin from tissues generally parallel the elimination from plasma.

Table 7: Mean (± SD) Cmax and AUC values following single and multiple doses of 400 mg moxifloxacin given orally

<table>
<thead>
<tr>
<th>Tissue or Fluid</th>
<th>Cmax (mcg/mL)</th>
<th>AUC (mcg•h/mL)</th>
<th>Half-life (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy young male (n = 15)</td>
<td>4.5 ± 0.5</td>
<td>48 ± 2.7</td>
<td>12.7 ± 1.9</td>
</tr>
<tr>
<td>Healthy elderly male (n = 8)</td>
<td>3.8 ± 0.3</td>
<td>51.8 ± 6.7</td>
<td>12.0 ± 0.7</td>
</tr>
<tr>
<td>Healthy elderly female (n = 8)</td>
<td>4.6 ± 0.6</td>
<td>54.6 ± 6.7</td>
<td>12.1 ± 0.7</td>
</tr>
<tr>
<td>Healthy young female (n = 8)</td>
<td>3.6 ± 0.5</td>
<td>48.2 ± 9</td>
<td>12.7 ± 1.9</td>
</tr>
</tbody>
</table>

Table 8: Mean (± SD) Cmax and AUC values following single and multiple doses of 400 mg moxifloxacin given by 1 hour intravenous infusion

<table>
<thead>
<tr>
<th>Tissue or Fluid</th>
<th>Cmax (mcg/mL)</th>
<th>AUC (mcg•h/mL)</th>
<th>Half-life (hr)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>3.8 ± 0.3</td>
<td>51.8 ± 6.7</td>
<td>12.0 ± 0.7</td>
</tr>
<tr>
<td>Healthy elderly female (n = 8)</td>
<td>4.6 ± 0.6</td>
<td>54.6 ± 6.7</td>
<td>12.1 ± 0.7</td>
</tr>
<tr>
<td>Healthy young female (n = 8)</td>
<td>3.6 ± 0.5</td>
<td>48.2 ± 9</td>
<td>12.7 ± 1.9</td>
</tr>
</tbody>
</table>

Mean steady-state plasma concentrations of moxifloxacin obtained with once daily dosing of 400 mg either orally (n=107) or by intravenous infusion (n=12)

Plasma concentrations increase proportionally with dose up to the highest dose tested (1200 mg single oral dose). The mean (± SD) elimination half-life from plasma is 12 ± 1.3 hours; steady-state is achieved after at least three days with a 400 mg once daily regimen.

A study of the skin response to ultraviolet (UVA and UVB) and visible radiation conducted in 32 healthy volunteers (8 per group) demonstrated that moxifloxacin does not show phototoxicity in comparison to placebo. The minimum erythematous dose (MED) was measured before and after treatment with moxifloxacin (200 mg or 400 mg once daily), lonefloxacin (400 mg once daily), or placebo. In this study, the MED measured for both doses of moxifloxacin were not significantly different from placebo, while lonefloxacin significantly lowered the MED. (See Warnings and Precautions (5.12)).
from warfarin did not significantly affect the pharmacokinetics of moxifloxacin. These results and the data from volunteer studies with cytochrome (CYP) P450 enzymes indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2.

**Excretion**

Approximately 45% of an oral or intravenous dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in feces). A total of 90% ± 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 1.8 ± 0.5 L/hr, respectively.

**Pharmacokinetics in Specific Populations**

**Geriatric**

Following oral administration of 400 mg moxifloxacin for 10 days in 16 elderly (8 male; 8 female) and 17 young (8 male; 9 female) healthy volunteers, there were no age-related changes in moxifloxacin pharmacokinetics. In 16 healthy male volunteers (8 young; 8 elderly) given a single 200 mg dose of oral moxifloxacin, the extent of systemic exposure (AUC and Cmax) was not statistically different between young and elderly males and elimination half-life was unchanged. No dosage adjustment is necessary based on age. In large phase III studies, the concentrations around the time of the end of the infusion in elderly patients following intravenous infusion of 400 mg were similar to those observed in young patients. [see Use In Specific Populations (8.5)]

**Gender**

Following oral administration of 400 mg moxifloxacin daily for 10 days to 23 healthy males (19 to 75 years) and 24 healthy females (19 to 70 years), the mean AUC and Cmax were 8% and 16% higher, respectively, in females compared to males. There are no significant differences in moxifloxacin pharmacokinetics between male and female subjects when differences in body weight are taken into consideration.

A 400 mg single dose study was conducted in 18 young males and females. The comparison of moxifloxacin pharmacokinetics in this study (9 young females and 9 young males) showed no differences in AUC or Cmax due to gender. Dosage adjustments based on gender are not necessary.

**Race**

Study-state moxifloxacin pharmacokinetics in male Japanese subjects were similar to those determined in Caucasian, with a mean Cmax of 4.1 mcg/mL, an AUC of 47 mcg•h/mL, and an elimination half-life of 14 hours, following 400 mg p.o. daily.

**Renal Insufficiency**

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).

In a single oral dose study of 24 patients with varying degrees of renal function from normal to severely impaired, the mean peak concentrations (Cmax) of moxifloxacin were reduced by 21% and 28% in the patients with moderate (CLcre=50 to 59 mL/min) and severe (CLcre<10 mL/min) renal impairment, respectively. The mean systemic exposure (AUC) in these patients was increased by 13%. In the moderate and severe renal impaired patients, the mean AUC for the sulfate conjugate (M1) increased by 1.7-fold (ranging up to 2.8-fold) and mean AUC and Cmax for the glucuronide conjugate (M2) increased by 2.8-fold (ranging up to 4.8-fold) and 1.4-fold (ranging up to 2.5-fold), respectively [See Use In Specific Populations (8.6)].

The pharmacokinetics of single dose and multiple dose moxifloxacin were studied in patients with CLcre<20 mL/min on either hemodialysis or continuous ambulatory peritoneal dialysis (8 HD, 8 CAPD).

Following a single 400 mg oral dose, the AUC of moxifloxacin in these HD and CAPD patients did not vary significantly from the AUC generally found in healthy volunteers. Cmax values of moxifloxacin were reduced by about 45% and 33% in HD and CAPD patients, respectively, compared to healthy, historical controls. The exposure (AUC) in the sulfate conjugate (M1) increased by 1.4-1.5-fold in these patients. The mean AUC of the glucuronide conjugate (M2) increased by a factor of 7.5, whereas the mean Cmax values of the glucuronide conjugate (M2) increased by a factor of 2.5 to 3, compared to healthy subjects. The sulfate and the glucuronide conjugates of moxifloxacin are not microbiologically active, and the clinical implication of increased exposure to these metabolites in patients with renal disease including those undergoing HD and CAPD has not been studied.

Oral administration of 400 mg QD moxifloxacin for 7 days to patients on HD or CAPD produced mean systemic exposure (AUC) to moxifloxacin similar to that generally seen in healthy volunteers. Steady-state Cmax values were about 22% lower in HD patients but were comparable between CAPD patients and healthy volunteers. Both HD and CAPD removed only small amounts of moxifloxacin from the body (approximately 9% by HD, and 3% by CAPD). HD and CAPD also removed about 4% and 2% of the glucuronide metabolite (M2), respectively.

**Hepatic Insufficiency**

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, moxifloxacin hydrochloride should be used with caution in these patients [see Warnings and Precautions (5.6) and Use In Specific Populations (8.7)].

In 400 mg single oral dose studies in 6 patients with mild (Child-Pugh Class A) and 10 patients with moderate (Child-Pugh Class B) hepatic insufficiency, moxifloxacin in mean systemic exposure (AUC) was 78% and 102%, respectively, of 18 healthy controls and mean peak concentration (Cmax) was 79% and 84% of controls.

The mean AUC of the sulfate conjugate of moxifloxacin (M1) increased by 3.9-fold (ranging up to 5.9-fold) and 5.7-fold (ranging up to 8-fold) in the mild and moderate groups, respectively. The mean Cmax of M1 increased by approximately 3-fold in both groups (ranging up to 4.7- and 3.5-fold). The mean AUC of the glucuronide conjugate of moxifloxacin (M2) increased by 1.5-fold (ranging up to 2.5-fold) in both groups. The mean Cmax of M2 increased by 1.6- and 1.3-fold (ranging up to 2.7- and 2.1-fold), respectively. The clinical significance of increased exposure to the sulfate and glucuronide conjugates has not been studied. In a subset of patients participating in a clinical trial, the plasma concentrations of moxifloxacin and metabolites determined approximately at the moxifloxacin T_max following the first intravenous or oral moxifloxacin hydrochloride dose in the Child-Pugh Class C patients (n=10) were similar to those in the Child-Pugh Class A/B patients (n=5), and also similar to those observed in healthy volunteer studies.

**Drug-Drug Interactions**

The following drug interactions were studied in healthy volunteers or patients.

Amoxicillin and iraconazole, morphine, phenobarbital, ranitidine, theophylline, cyclosporine and warfarin did not significantly affect the pharmacokinetics of moxifloxacin. These results and the data from in vitro studies suggest that moxifloxacin is unlikely to significantly alter the metabolic clearance.
Moxifloxacin has been shown to be active against most isolates of the following bacteria, both negative and positive bacteria. There is no known cross-resistance between moxifloxacin and other fluoroquinolones against Gram-negative bacteria. Gram-positive bacteria resistant to other fluoroquinolones may, however, still be susceptible to moxifloxacin.

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.


drug interactions


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antimicrobial activity

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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.

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-mutation. resistance to moxifloxacin occurs in vitro at a general frequency of between 1.8 x 10^-8 to < 1 x 10^-11 for gram-positive bacteria.

cross-resistance

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oral contraceptives

moxifloxacin had no clinically significant effect on the pharmacokinetics of levonorgestrel/0.03 mg ethinylestradiol (as measured by serum progesterone, fsh, estradiol, and lh), or with the pharmacokinetics of the administered contraceptive agent.

probenecid

no significant effect of probenecid (500 mg twice daily for two days) on the pharmacokinetics of moxifloxacin (400 mg single dose) was detected in a study involving 12 healthy volunteers. the mean auc and c_{max} of moxifloxacin were reduced by 12% and 18%, respectively.

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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, ceftazidime), 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**
- Chlamydia 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 against isolates of similar genus or organism group. However, the efficacy of moxifloxacin 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

**Gram-negative bacteria**
- Citrobacter freundii
- Klebsiella oxytoca
- Legionella pneumophila

**Anaerobic bacteria**
- Fusobacterium species
- Prevotella species

### Susceptibility Test 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).

#### 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 (diameter) should be determined using a standardized test method. **The MIC values should be interpreted according to the criteria in Table 10.**

#### Anaerobic Techniques

For anaerobic bacteria, the susceptibility to moxifloxacin can be determined by a standardized test method. **The MIC values obtained should be interpreted according to the criteria provided in Table 10.**

---

**Table 10: Susceptibility Test Interpretive Criteria for Moxifloxacin**

<table>
<thead>
<tr>
<th>Species</th>
<th>MIC (mcg/mL)</th>
<th>Zone Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>≤2</td>
<td>≥4</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>≤1</td>
<td>≥2</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>≤0.5</td>
<td>1</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>≤1</td>
<td>≥2</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae</td>
<td>≤1</td>
<td>≥2</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>≤1</td>
<td>2</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>≤2</td>
<td>4</td>
</tr>
<tr>
<td>Yersinia pestis</td>
<td>≤0.25</td>
<td>-</td>
</tr>
</tbody>
</table>

S=susceptible, I=Intermediate, and R=Resistant.

**The current absence of data on moxifloxacin-resistant isolates precludes defining any results other than “susceptible”. Isolates yielding test results (MIC or zone diameter) other than susceptible, should be submitted to a reference laboratory for additional testing.**

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 results should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category applies 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. Standardized moxifloxacin powder should provide the following range of MIC values noted in Table 11. For the diffusion technique using the 5 mcg moxifloxacin disk, the criteria in Table 11 should be achieved.

#### Table 11: Acceptable Quality Control Ranges for Moxifloxacin

<table>
<thead>
<tr>
<th>Strains</th>
<th>MIC range (mcg/mL)</th>
<th>Zone Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecalis ATCC 29212</td>
<td>0.06 to 0.5</td>
<td>20/23 (87%)</td>
</tr>
<tr>
<td>Echerichia coli ATCC 25922</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Haemophilus influenzae ATCC 49247</td>
<td>0.008 to 0.03</td>
<td>31</td>
</tr>
<tr>
<td>Supplyfuscosus naurus ATCC 29213</td>
<td>0.015 to 0.12</td>
<td>31</td>
</tr>
<tr>
<td>Supplyfuscosus naurus ATCC 29213</td>
<td>0.06 to 0.25</td>
<td>31</td>
</tr>
<tr>
<td>Streptococcus pneumoniae ATCC 49619</td>
<td>0.125 to 0.5</td>
<td></td>
</tr>
<tr>
<td>Bacteroides fragilis ATCC 25285</td>
<td>1 to 4</td>
<td></td>
</tr>
<tr>
<td>Bacteroides thetaiomicron ATCC 29741</td>
<td>0.125 to 0.5</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli ATCC 25922</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Enterococcus faecalis ATCC 25285</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Enterococcus faecalis ATCC 25285</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 29213</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 29213</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 29213</td>
<td>0.008 to 0.06</td>
<td>28</td>
</tr>
</tbody>
</table>

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. Moxifloxacin was not mutagenic in 4 bacterial strains (TA 98, TA 100, TA 1535, TA 1537) used in the Ames Salmonella reversion assay. As with other fluoroquinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when V79 cells were used in a clastogenic in vitro chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity in vivo in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 12 times the maximum recommended human dose based on body surface area (BSA) or at intravenous doses as high as 45 mg/kg/day, approximately equal to the maximum recommended human dose based on body surface area. At 500 mg/kg orally there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

#### 13.2 Animal Toxicology and/or Pharmacology

Fluoroquinolones have been shown to cause arthropathy in immature animals. In studies in juvenile dogs oral doses of moxifloxacin 30 mg/kg/day or more (approximately 1.5 times the maximum recommended human dose based on BSA) resulted in arthropathy. There was no evidence of arthropathy in mature monkeys and rats at oral doses up to 135 and 500 mg/kg/day, respectively. Moxifloxacin at an oral dose of 300 mg/kg did not show an increase in acute toxicity or potential for CNS toxicity (for example, seizures) in mice when used in combination with NSAIDs such as diclofenac, ibuprofen, or fenbufen. Some fluoroquinolones have been reported to have proconvulsant activity that is exacerbated with concomitant use of NSAIDs.

A QT-prolonging effect of moxifloxacin was found in dog studies, at plasma concentrations about five times the human therapeutic level. The combined infusion of sotalol, a Class III antiarrhythmic agent, with moxifloxacin induced a higher degree of QTc prolongation in dogs than that induced by the same dose (30 mg/kg) of moxifloxacin alone. Electrophysiological in vitro studies suggested an inhibition of the rapid activating component of the delayed rectifier potassium current (I_{Kr}) as an underlying mechanism.

No sign of local intolerability were observed in dogs when moxifloxacin was administered intravenously. After intra-arterial injection, inflammatory changes involving the peri-arterial soft tissue were observed.

#### 14 CLINICAL STUDIES

##### 14.1 Acute Bacterial Sinusitis

In a controlled double-blind study conducted in the US, moxifloxacin hydrochloride tablets (400 mg once daily for five days) were compared with cefuroxime axetil (250 mg twice daily for five days) for the treatment of acute bacterial sinusitis. The trial included 457 patients valid for the efficacy analysis. Clinical success at 7 to 21 days post-therapy test of cure visit was 90% for moxifloxacin 400 mg once daily for ten days) were compared with cefuroxime axetil (250 mg twice daily for ten days) for the treatment of acute bacterial exacerbation of chronic bronchitis. This study compared moxifloxacin hydrochloride (500 mg twice daily for 10 days) and enrolled 629 patients. Clinical success was assessed at 7 to 17 days post-therapy. The clinical success for moxifloxacin hydrochloride was 89% (222/250) compared to 89% (224/251) for clarithromycin.

#### Table 12: Clinical Success Rates at Follow-Up Visit for Clinically Evaluable Patients by Pathogen (Acute Bacterial Exacerbation of Chronic Bronchitis)

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>Moxifloxacin Hydrochloride</th>
<th>Clarithromycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>16/16 (100%)</td>
<td>16/16 (100%)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>33/37 (92%)</td>
<td>36/41 (88%)</td>
</tr>
</tbody>
</table>
The microbical eradication rates (eradication plus presumed eradication) in moxifloxacin treated patients were Streptococcus pneumoniae 100%, Haemophilus influenzae 89%, Haemophilus parainfluenzae 100%, Moraxella catarrhalis 85%, Staphylococcus aureus 94%, and Klebsiella pneumoniae 83%.

14.3 Community Acquired Pneumonia

A randomized, double-blind, controlled clinical trial conducted in the US compared the efficacy of moxifloxacin hydrochloride tablets (400 mg once daily) to that of high-dose clarithromycin (500 mg twice daily) in the treatment of patients with clinically and radiologically documented community acquired pneumonia. This study enrolled 474 patients (282 of whom were valid for the efficacy analysis conducted at the 14 to 35 day follow-up visit). Clinical success for clinically evaluable patients was 95% (184/194) for moxifloxacin hydrochloride and 93% (178/188) for high dose clarithromycin.

A randomized, double-blind, controlled clinical trial was conducted in the US and Canada to compare the efficacy of sequential intravenous/oral moxifloxacin 400 mg once a day for 7 to 14 days to an intravenous/oral beta-lactam/beta-lactamase inhibitor control in the treatment of patients with clinically and radiologically documented community acquired pneumonia. This study enrolled 516 patients, 362 of whom were valid for the efficacy analysis conducted at the 7 to 30 day post-therapy visit. The clinical success rate was 88% (370/418) for moxifloxacin hydrochloride therapy and 89% (161/180) for the fluoroquinolone comparators.

The clinical success rates by pathogen across the four CAP studies are presented in Table 13.

### Table 13: Clinical Success Rates By Pathogen (Pooled CAP Studies)

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>Moxifloxacin Hydrochloride</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>100% (95%)</td>
<td>96% (95%)</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>92% (92%)</td>
<td>92% (92%)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>89% (89%)</td>
<td>85% (85%)</td>
</tr>
<tr>
<td>Chlamydia pneumonia</td>
<td>93% (93%)</td>
<td>93% (93%)</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>96% (96%)</td>
<td>93% (93%)</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>92% (92%)</td>
<td>92% (92%)</td>
</tr>
</tbody>
</table>

Community Acquired Pneumonia caused by Multi-Drug Resistant Streptococcus pneumoniae (MDRSP)*

Moxifloxacin hydrochloride was effective in the treatment of community acquired pneumonia (CAP) caused by multi-drug resistant Streptococcus pneumoniae MDRSP** isolates. Of 37 microbiologically evaluable patients with MDRSP isolates, 35 patients (95%) achieved clinical and bacteriological success post-therapy. The clinical and bacteriological success rates based on the number of patients treated are shown in Table 14.

### Table 14: Clinical and Bacteriological Success Rates for Moxifloxacin-Treated MDRSP*** CAP Patients (Population Valid for Efficacy)

<table>
<thead>
<tr>
<th>Screening Susceptibility</th>
<th>Clinical Success</th>
<th>Bacteriological Success</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
</tr>
<tr>
<td>Penicillin-resistant</td>
<td>21/21 (100%)</td>
<td>21/21 (100%)</td>
</tr>
<tr>
<td>2nd generation cephalosporin-resistant</td>
<td>25/26 (96%)</td>
<td>25/26 (96%)</td>
</tr>
<tr>
<td>Macrolide-resistant</td>
<td>22/23 (96%)</td>
<td>22/23 (96%)</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole-resistant</td>
<td>28/30 (93%)</td>
<td>28/30 (93%)</td>
</tr>
<tr>
<td>Tetracycline-resistant</td>
<td>17/18 (94%)</td>
<td>17/18 (94%)</td>
</tr>
</tbody>
</table>

a) n = number of patients successfully treated; N = number of patients with MDRSP (from a total of 37 patients)
b) n = number of patients successfully treated (presumed eradication or eradication);

Not all isolates were resistant to all antimicrobial classes tested. Success and eradication rates are summarized in Table 15.

### Table 15: Clinical Success Rates and Microbiological Eradication Rates for Resistant Streptococcus pneumoniae (Community Acquired Pneumonia)

<table>
<thead>
<tr>
<th>S. pneumoniae with MDRSP</th>
<th>Clinical Success</th>
<th>Bacteriological Eradication Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resist to 2 antimicrobials</td>
<td>12/13 (92.3%)</td>
<td>12/13 (92.3%)</td>
</tr>
<tr>
<td>Resist to 3 antimicrobials</td>
<td>10/11 (90.9%)</td>
<td>10/11 (90.9%)</td>
</tr>
<tr>
<td>Resist to 4 antimicrobials</td>
<td>6/6 (100%)</td>
<td>6/6 (100%)</td>
</tr>
<tr>
<td>Resist to 5 antimicrobials</td>
<td>7/7 (100%)</td>
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Not all isolates were resistant to all antimicrobial classes tested. Success and eradication rates are summarized in Table 15.

**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.

### Table 14: Clinical and Bacteriological Success Rates for Moxifloxacin-Treated MDRSP*** CAP Patients (Population Valid for Efficacy)

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<td>Resist to 5 antimicrobials</td>
<td>7/7 (100%)</td>
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</table>

b) One patient had a respiratory isolate resistant to 5 antimicrobials and a blood isolate resistant to 3 antimicrobials. The patient was included in the category resistant to 5 antimicrobials.

14.4 Uncomplicated Skin and Skin Structure Infections

A randomized, double-blind, controlled clinical trial conducted in the US compared the efficacy of moxifloxacin 400 mg once daily for seven days with cephalexin HCI 500 mg three times daily for seven days. The percentage of patients treated for uncomplicated abscesses was 30%, furuncles 8%, cellulitis 16%, impetigo 20%, and other skin infections 26%.

Adverse procedures (mixin and drainage or debridement) were performed on 17% of the moxifloxacin hydrochloride treated patients and 14% of the comparator treated patients. Clinical success rates in evaluable patients were 99% (108/112) for moxifloxacin hydrochloride and 91% (110/122) for cephalexin HCI.

14.5 Complicated Skin and Skin Structure Infections

Two randomized, active controlled trials of cSSSI were performed. A double-blind trial was conducted primarily in North America to compare the efficacy of sequential intravenous/oral moxifloxacin 400 mg once a day for 7 to 14 days to an intravenous/oral beta-lactam/beta-lactamase inhibitors control in the treatment of patients with cSSSI. This study enrolled 617 patients, 335 of which were valid for the
efficacy analysis. A second open-label international study compared moxifloxacin 400 mg once a day for 7 to 21 days in sequential intravenous/oral beta-lactam-beta-lactamase inhibitor control in the treatment of patients with cSSSI. This study enrolled 681 patients, 62% of which were valid for the efficacy analysis. Surgical incision and drainage or debridement was performed on 55% of the moxifloxacin hydrochloride treated and 53% of the comparator treated patients in these studies and formed an integral part of therapy for this indication. Success rates varied with the type of diagnosis ranging from 61% in patients with infected ulcers to 90% in patients with complicated empyelas. These rates were similar to those seen with comparator drugs. The overall success rates in the evaluable patients and the clinical success by pathogen are shown in Tables 16 and 17.

### 14.6 Complicated Intra-Abdominal Infections

Two randomized, controlled trials of cIAI were performed. A double-blind trial was conducted primarily in North America to compare the efficacy of sequential intravenous/oral moxifloxacin 400 mg once a day for 5 to 14 days to intravenous/piperacillin/tazobactam followed by oral amoxicillin/clavulanic acid in the treatment of patients with cIAI, including peritonitis, abscesses, appendicitis with perforation, and bowel perforation. This study enrolled 681 patients, 279 of which were considered clinically evaluable. A second open-label international study compared moxifloxacin 400 mg once a day for 5 to 14 days to intravenous ceftriaxone plus intravenous menadione sodium bisulfite followed by oral amoxicillin/clavulanic acid in the treatment of patients with cIAI. This study enrolled 595 patients, 311 of which were considered clinically evaluable. The clinically evaluable population consisted of subjects with a surgically confirmed complicated infection, at least 5 days of treatment and a 25 to 50 day follow-up assessment for patients at the Test of Cure visit. The overall clinical success rates in the clinically evaluable patients are shown in Table 18.

### 14.7 Plague

Efficacy studies of moxifloxacin hydrochloride could not be conducted in humans with pneumonic plague for ethical and feasibility reasons. Therefore, approval of this indication was based on an efficacy study conducted in animals and supportive pharmacokinetic data in adult humans and animals. A randomized, blinded, placebo-controlled study was conducted in an African Green Monkey (AGM) animal model of pneumonic plague. Twenty AGM (10 males and 10 females) were exposed to an inhaled strain used in this study was 0.06 mcg/mL. Development of sustained fever for at least 4 hours duration was used as the trigger for the initiation of 10 days of treatment with either a hematuria regimen of moxifloxacin or placebo. All study animals were febrile and bacteremic with Y. pestis prior to the initiation of study treatment. Ten of 10 (100%) of the animals receiving the placebo succumbed to disease between 83 to 139 h (mean 115 ± 19 hours) post-treatment. Ten of 10 (100%) moxifloxacin-treated animals survived for the 38-day period after completion of the study treatment. Compared to the placebo group, mortality in the moxifloxacin group was significantly lower (difference in survival: 100% with a two-sided 95% exact confidence interval –9.4%, 2.2%).

The mean plasma concentrations of moxifloxacin associated with a statistically significant improvement in survival over placebo in an AGM model of pneumonic plague were reached or exceeded in human adults receiving the recommended oral and intravenous dosage regimen. The mean (± SD) peak plasma concentration (Cmax) and trough plasma exposure defined as the area under the plasma concentration-time curve (AUC) in human adults receiving 400 mg intravenously were 3.8 ± 0.3 mcg/mL and 39.3 ± 8.6 mcg·h/mL, respectively [see Clinical Pharmacology (12.2)]. The mean (± SD) peak plasma concentration and AUC0-24 in AGM following one-day administration of a hematuria dosing regimen simulating the human AUC0-24 of a 400 mg dose were 4.4 ± 1.5 mcg/mL and 22 ± 8.8 mcg·h/mL, respectively.

#### Tables

<table>
<thead>
<tr>
<th>Table 16: Overall Clinical Success Rates in Patients with Complicated Skin and Skin Structure Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>North America (overall)</td>
</tr>
<tr>
<td>Abscess</td>
</tr>
<tr>
<td>Non-abscess</td>
</tr>
<tr>
<td>International (overall)</td>
</tr>
<tr>
<td>Abscess</td>
</tr>
<tr>
<td>Non-abscess</td>
</tr>
<tr>
<td>a) of difference in success rates between Moxifloxacin and comparator (Moxifloxacin – comparator)</td>
</tr>
<tr>
<td>b) Excludes 2 patients who required additional surgery within the first 48 hours.</td>
</tr>
<tr>
<td>c) NA – not applicable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 17: Clinical Success Rates by Pathogen in Patients with Complicated Skin and Structure Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (methicillin-susceptible isolate)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
</tr>
<tr>
<td>a) methicillin susceptibility was only determined in the North American Study</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 18: Clinical Success Rates in Patients with Complicated Intra-Abdominal Infections</th>
</tr>
</thead>
<tbody>
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</tr>
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<td>---</td>
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</tr>
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<td>a) of difference in success rates between moxifloxacin hydrochloride and comparator (moxifloxacin hydrochloride – comparator)</td>
</tr>
<tr>
<td>b) Excludes 2 patients who required additional surgery within the first 48 hours.</td>
</tr>
<tr>
<td>c) NA – not applicable</td>
</tr>
</tbody>
</table>

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 Moxifloxacin Hydrochloride Tablets
Moxifloxacin hydrochloride tablets 400 mg are available as light pink colored, capsule shaped biconvex film-coated tablets debossed with “L01” on one side and “488” on other side.

Package

| Bottles of 30 | NDC 13668-201-30 |
| Bottles of 100 | NDC 13668-201-01 |
| Bottles of 500 | NDC 13668-201-45 |

Storage: Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Avoid high humidity.

17 PATIENT COUNSELING INFORMATION

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

Serious Adverse Reactions

Advises patients to stop taking moxifloxacin hydrochloride tablets if they experience an adverse reaction and to call their health-care 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 moxifloxacin hydrochloride tablets or other fluoroquinolones:

- **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 moxifloxacin hydrochloride tablets and may occur together in the same patient. Inform patients to stop taking moxifloxacin hydrochloride tablets 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 moxifloxacin hydrochloride tablets treatment.

- **Peripheral Neuropathies:** Inform patients that peripheral neuropathies have been associated with moxifloxacin hydrochloride use, symptoms may occur soon after initiation of therapy and may be irreversible. Inform patients that symptoms of peripheral neuropathy including pain, burning, tingling, numbness and/or weakness develop, immediately discontinue moxifloxacin hydrochloride 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 moxifloxacin hydrochloride. 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 moxifloxacin hydrochloride 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 moxifloxacin hydrochloride can cause hypersensitivity reactions, even after a single dose, and to discontinue the drug at the first sign of skin rash, hives or other skin reactions, a rapid heartbeat, difficulty in swallowing or breathing, any swelling suggesting angioneurotic (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 moxifloxacin hydrochloride tablets. 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.

- **Diabetes:** Diabetes is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop excessive thirst and increased urination. Inform patients to develop a steady diet and to control their diabetes as much as possible.

- **Prolongation of the QT Interval:** Instruct patients to inform their physician of any personal or family history of QT prolongation or paroxysmal tachycardia, or recent myocardial infarction; 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/Photositivity:** Inform patients that photosensitivity/phototoxicity has been reported in patients receiving fluoroquinolones. Instruct patients to minimize or avoid exposure to natural or artificial sunlight (facing sunburning beds or UV/A/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 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 moxifloxacin hydrochloride tablets and consult a physician.

Antibacterial Resistance

Inform patients that antibacterial drugs including moxifloxacin hydrochloride should only be used to treat bacterial infections. They do not treat viral infections (for example, the common cold). When moxifloxacin hydrochloride tablets are prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by moxifloxacin hydrochloride or other antibacterial drugs in the future.

Administration With Food, Fluids, and Drug Products Containing Multivalent Cations

Inform patients that moxifloxacin hydrochloride tablets may be taken with or without food. Advise patients drink fluids liberally.

Inform patients that moxifloxacin hydrochloride tablets should be taken at least 4 hours before or 8 hours after multivitamins (containing iron or zinc), cations (containing magnesium or aluminum), sucralfate, or didanosine buffered tablets for oral suspension or the pediatric powder for oral solution.

Plague Studies

Inform patients given moxifloxacin hydrochloride for plague that efficacy studies could not be conducted in humans for feasibility reasons. Therefore, approval for plague was based on efficacy studies conducted in animals.

Manufactured by:
TORRENT PHARMACEUTICALS LTD., Indrad-382 721, Dist. Mehsana, INDIA.
Moxifloxacin hydrochloride tablets should not be used in patients with acute bacterial sinusitis or acute bacterial exacerbation of chronic bronchitis.

Moxifloxacin hydrochloride tablets are a fluoroquinolone antibiotic medicine used to treat certain types of infections caused by certain germs called bacteria in adults 18 years or older. These bacterial infections include:

- Community Acquired Pneumonia
- Uncomplicated Skin and Skin Structure Infections
- Complicated Skin and Skin Structure Infections
- Complicated Intra-Abdominal Infections
- Plague
- Acute Bacterial S在一属
- Acute Bacterial Exacerbation of Chronic Bronchitis

Moxifloxacin hydrochloride tablets should not be used in patients with acute bacterial sinusitis or acute bacterial exacerbation of chronic bronchitis.

What is the most important information I should know about moxifloxacin hydrochloride tablets?

Moxifloxacin hydrochloride tablets belong to a class of antibiotics called fluoroquinolones. Moxifloxacin hydrochloride tablets can cause serious side effects that can happen at the same time and could result in death. If you get any of the following serious side effects, you should stop taking moxifloxacin hydrochloride tablets and get medical help right away:

- Tendon rupture or swelling of the tendon (tendinitis),
- Tendinitis that happens on the back of your ankle, or Achilles,
- Severe blood in the eye
- Headache that does not go away, with or without blurred vision
- Sudden severe vision changes
- Changes in sensation and possible nerve damage (Peripheral Neuropathy)

Tendinitis or tendon rupture may also happen with other fluoroquinolone antibacterial medicines, including moxifloxacin hydrochloride tablets. Tell your healthcare provider about whether you should continue to take moxifloxacin hydrochloride tablets.

1. Tendon problems in people who take moxifloxacin hydrochloride tablets:

- Tendon problems can happen in people of all ages who take moxifloxacin hydrochloride tablets. Tendons are tough cords of tissue that connect muscles to bones. Symptoms of tendon problems may include:
  - Pain, swelling, or inflammation of the tendon
  - Bruising right after an injury in a tendon area
  - Hear or feel a snap or pop in a tendon area
  - Bruising right after an injury in a tendon area
  - Unable to move the affected area or bear weight.

Moxifloxacin hydrochloride tablets may need to be stopped to prevent permanent nerve damage.

2. Changes in sensation and possible nerve damage (Peripheral Neuropathy). Damage to the nerves in arms, hands, legs, or feet can happen in people who take fluoroquinolones, including moxifloxacin hydrochloride tablets. Tell your healthcare provider if you have a history of fluoroquinolone use before starting or when you stop taking moxifloxacin hydrochloride tablets. CNS side effects may happen as soon as after taking the first dose of moxifloxacin hydrochloride tablets. CNS side effects may include:

- Seizures
- Sudden severe vision changes
- Changes in sensation and possible nerve damage (Peripheral Neuropathy)

3. Central Nervous System (CNS) effects. Seizures have been reported in people who take fluoroquinolone antibacterial medicines, including moxifloxacin hydrochloride tablets. Tell your healthcare provider if you have a history of seizures before you start taking moxifloxacin hydrochloride tablets. Tell your healthcare provider if you have a history of myasthenia gravis before you start taking moxifloxacin hydrochloride tablets. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problems.

4. Worsening of myasthenia gravis (a disease which causes muscle weakness).

Fluoroquinolones like moxifloxacin may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Tell your healthcare provider if you have a history of myasthenia gravis before you start taking moxifloxacin hydrochloride tablets. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problems.

See the section “What are the possible side effects of moxifloxacin hydrochloride tablets?” for more information about side effects.

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Rx Only

Read the Medication Guide that comes with moxifloxacin hydrochloride tablets before you start taking them and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment.

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2. Changes in sensation and possible nerve damage (Peripheral Neuropathy). Damage to the nerves in arms, hands, legs, or feet can happen in people who take fluoroquinolones, including moxifloxacin hydrochloride tablets. Tell your healthcare provider if you have a history of fluoroquinolone use before starting or when you stop taking moxifloxacin hydrochloride tablets. CNS side effects may happen as soon as after taking the first dose of moxifloxacin hydrochloride tablets. CNS side effects may include:

- Seizures
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4. Worsening of myasthenia gravis (a disease which causes muscle weakness).

Fluoroquinolones like moxifloxacin may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Tell your healthcare provider if you have a history of myasthenia gravis before you start taking moxifloxacin hydrochloride tablets. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problems.

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- Acute Bacterial Exacerbation of Chronic Bronchitis

Moxifloxacin hydrochloride tablets should not be used in patients with acute bacterial sinusitis or acute bacterial exacerbation of chronic bronchitis.
bacterial exacerbation of chronic bronchitis if there are other treatment options available.

Studies of moxifloxacin hydrochloride for use in the treatment of plague were done in animals only, because plague could not be studied in people.

It is not known if moxifloxacin hydrochloride tablets are safe and work in people under 18 years of age. Children have a higher chance of getting bone, joint, and tendon (musculoskeletal) problems while taking fluoroquinolone antibiotic medicines.

Sometimes infections are caused by viruses rather than by bacteria. Examples include viral infections in the sinuses and lungs, such as the common cold or flu. Antibiotics, including moxifloxacin hydrochloride tablets, do not kill viruses.

Call your healthcare provider if you think your condition is not getting better while you are taking moxifloxacin hydrochloride tablets.

Who should not take moxifloxacin hydrochloride tablets?

Do not take moxifloxacin hydrochloride tablets if you have ever had a severe allergic reaction to an antibiotic known as a fluoroquinolone, or if you are allergic to any of the ingredients in moxifloxacin hydrochloride tablets. Ask your healthcare provider if you are not sure. See the list of ingredients in moxifloxacin hydrochloride tablets at the end of this Medication Guide.

What should I tell my healthcare provider before taking moxifloxacin hydrochloride tablets?

See “What is the most important information I should know about moxifloxacin hydrochloride tablets”.

Tell your healthcare provider about all your medical conditions, including if you:
- Have tendon problems; moxifloxacin hydrochloride tablets should not be used in patients who have a history of tendon problems.
- Have a disease that causes muscle weakness (myasthenia gravis); moxifloxacin hydrochloride tablets should not be used in patients who have a history of myasthenia gravis.
- Have central nervous system problems (such as epilepsy).
- Have nerve problems; moxifloxacin hydrochloride tablets should not be used in patients who have a history of a nerve problem called peripheral neuropathy.
- Have or anyone in your family has an irregular heartbeat, especially a condition called "QT prolongation".
- Have low blood potassium (hypokalemia).
- Have a slow heartbeat (bradycardia).
- Have a history of seizures.
- Have kidney problems.
- Have rheumatoid arthritis (RA) or other history of joint problems.
- Are pregnant or planning to become pregnant. It is not known if moxifloxacin hydrochloride tablets will harm your unborn child.
- Are breast-feeding or planning to breast-feed. It is not known if moxifloxacin hydrochloride passes into breast milk. You and your healthcare provider should decide whether you will take moxifloxacin hydrochloride tablets or breast-feed.
- Have diabetes or problems with low blood sugar (hypoglycemia).

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal and dietary supplements. Moxifloxacin hydrochloride tablets and other medicines can affect each other causing side effects. Especially tell your healthcare provider if you take:
- An NSAID (Non-Steroidal Anti-Inflammatory Drug). Many common medicines for pain relief are NSAIDs. Taking an NSAID while you take moxifloxacin hydrochloride tablets or other fluoroquinolones may increase your risk of central nervous system effects and seizures. See “What are the possible side effects of moxifloxacin hydrochloride tablets?”.  
- A blood thinner (warfarin, Coumadin, Jantoven).
- A medicine to control your heart rate or rhythm (antiarrhythmic). See “What are the possible side effects of moxifloxacin hydrochloride tablets?”.
- An anti-psychotic medicine.
- A tricyclic antidepressant.
- A medicine to control your heart rate or rhythm (antiarrhythmic). See “What are the possible side effects of moxifloxacin hydrochloride tablets?”.
- A water pill (diuretic).
- A steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury, See “What is the most important information I should know about moxifloxacin hydrochloride tablets?”.
- Certain medicines may keep moxifloxacin hydrochloride tablets from working correctly. Take moxifloxacin hydrochloride tablets either 4 hours before or 8 hours after taking these products:
  - An antacid, multivitamin, or other product that has magnesium, aluminum, iron, or zinc.
  - Sucralfate (Carafate®).
  - Didanosine oral suspension or solution.

Ask your healthcare provider if you are not sure if any of your medicines are listed above.

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take moxifloxacin hydrochloride tablets?

Take moxifloxacin hydrochloride tablets once a day exactly as prescribed by your healthcare provider.

- Take moxifloxacin hydrochloride tablets at the same time each day.
- Moxifloxacin hydrochloride tablets should be swallowed.
- Moxifloxacin hydrochloride tablets can be taken with or without food.
- Drink plenty of fluids while taking moxifloxacin hydrochloride tablets.
- Do not skip any doses, or stop taking moxifloxacin hydrochloride tablets even if you begin to feel better, until you finish your prescribed treatment, unless:
  - You have tendon problems (see “What is the most important information I should know about moxifloxacin hydrochloride tablets?”).
  - You have nerve problems. See “What is the most important information I should know about moxifloxacin hydrochloride tablets?”.
  - You have central nervous system problems. See “What is the most important information I should know about moxifloxacin hydrochloride tablets?”.
  - You have a serious allergic reaction (see “What are the possible side effects of moxifloxacin hydrochloride tablets?”), or your healthcare provider tells you to stop.
  - This will help make sure that all of the bacteria are killed and lower the chance that the bacteria will become resistant to moxifloxacin hydrochloride tablets. If this happens, moxifloxacin hydrochloride tablets and other antibiotic medicines may not work in the future.
  - If you miss a dose of Moxifloxacin hydrochloride tablets, take it as soon as you remember. Do not take more than 1 dose of moxifloxacin hydrochloride tablets in one day.
  - If you take too much, call your healthcare provider or get medical help immediately.

What should I avoid while taking moxifloxacin hydrochloride tablets?

- Moxifloxacin hydrochloride tablets can make you feel dizzy and lightheaded. Do not drive, operate machinery, or do other activities that require mental alertness or coordination until you know how moxifloxacin hydrochloride tablets affect you.
- Avoid sunlamps, tanning beds, and try to limit your time in the sun. Moxifloxacin hydrochloride tablets can make your skin sensitive to the sun (photosensitivity) and the light from sunlamps and tanning beds. You could get severe sunburn, blisters or swelling of your skin. If you get any of these symptoms while taking moxifloxacin hydrochloride tablets, call your healthcare provider right away. You should use a sunscreen and wear a hat and clothes that cover your skin if you have to be in sunlight.

What are the possible side effects of moxifloxacin hydrochloride tablets?

Moxifloxacin hydrochloride tablets can cause side effects that may be serious or even cause death. See “What is the most important information I should know about moxifloxacin hydrochloride tablets?”.
Other serious side effects of moxifloxacin hydrochloride tablets include:

**Serious allergic reactions**
- Allergic reactions can happen in people taking fluoroquinolones, including moxifloxacin hydrochloride tablets, even after only one dose. Stop taking moxifloxacin hydrochloride tablets and get emergency medical help right away if you get any of the following symptoms of a severe allergic reaction:
  - Hives
  - Trouble breathing or swallowing
  - Swelling of the lips, tongue, face
  - Throat tightness, hoarseness
  - Rapid heartbeat
  - Faint
  - Yellowing of the skin or eyes. Stop taking moxifloxacin hydrochloride tablets and tell your healthcare provider right away if you get yellowing of your skin or white part of your eyes, or if you have dark urine. These can be signs of a serious reaction to moxifloxacin hydrochloride tablets (a liver problem).

**Skin rash**
- Skin rash may happen in people taking moxifloxacin hydrochloride tablets even after only one dose. Stop taking moxifloxacin hydrochloride tablets and call your healthcare provider. Skin rash may be a sign of a more serious reaction to moxifloxacin hydrochloride tablets.

**Serious heart rhythm changes (QT prolongation and torsade de points)**
- Tell your healthcare provider right away if you have a change in your heart beat (a fast or irregular heartbeat), or if you faint. Moxifloxacin hydrochloride tablets may cause a rare heart problem known as prolongation of the QT interval. This condition can cause an abnormal heartbeat and can be very dangerous. The chances of this event are higher in people:
  - Who are elderly
  - With a family history of prolonged QT interval
  - With low blood potassium (hypokalemia)
  - Who take certain medicines to control heart rhythm (antiarrhythmics)

**Intestinal infection (Pseudomembranous colitis)**
- Pseudomembranous colitis can happen with most antibiotics, including moxifloxacin hydrochloride tablets. Call your healthcare provider right away if you get watery diarrhea, diarrhea that does not go away, or bloody stools. You may have stomach cramps and a fever. Pseudomembranous colitis can happen 2 or more months after you have finished your antibiotic.

**Changes in blood sugar**
- People who take moxifloxacin hydrochloride tablets and other fluoroquinolone medicines with oral anti-diabetes medicines or with insulin can get low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia). Follow your healthcare provider’s instructions for how often to check your blood sugar. If you have diabetes and you get low blood sugar while taking moxifloxacin hydrochloride tablets, stop taking moxifloxacin hydrochloride tablets and call your healthcare provider right away. Your antibiotic medicine may need to be changed.

**Sensitivity to sunlight (photosensitivity)**
- See “What should I avoid while taking moxifloxacin hydrochloride tablets?” The most common side effects of moxifloxacin hydrochloride tablets include nausea and diarrhea.

These are not all the possible side effects of moxifloxacin hydrochloride tablets. Tell your healthcare provider about any side effect that bothers you or that does not go away. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store moxifloxacin hydrochloride tablets?**
- Store moxifloxacin hydrochloride tablets at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F). Use USP Controlled Room Temperature.
- Keep moxifloxacin hydrochloride tablets away from moisture (humidity).

**General Information about Moxifloxacin Hydrochloride Tablets**
- Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use moxifloxacin hydrochloride tablets for a condition for which it is not prescribed. Do not give moxifloxacin hydrochloride tablets to other people, even if they have the same symptoms that you have. It may harm them.
- This Medication Guide summarizes the most important information about moxifloxacin hydrochloride tablets. If you would like more information about moxifloxacin hydrochloride tablets, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about moxifloxacin hydrochloride tablets that is written for healthcare professionals. For more information call 1-866-481-0108.

**What are the ingredients in moxifloxacin hydrochloride tablets?**
- Moxifloxacin hydrochloride tablets:
  - Active ingredient: moxifloxacin hydrochloride, USP
  - Inactive ingredients: colloidial silicon dioxide, croscarmellose sodium, ferric oxide red, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol 400, polyvinyl pyrrolidone, pregelatinised starch and titanium dioxide.

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This Medication Guide has been approved by the U.S. Food and Drug Administration.
## MOXIFLOXACIN HYDROCHLORIDE

### Product Information

**Product Type**: HUMAN PRESCRIPTION DRUG  
**Item Code (Source)**: NDC:13668-201-01

### Route of Administration

**ORAL**

### Active Ingredient/Active Moiety

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### Inactive Ingredients

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### Product Characteristics

**Color**  
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**Score**  
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**Size**  
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**Flavor**  
Imprint Code: 1201  
**Contains**  
Contains

### Packaging

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### Marketing Information

**Labeler**  
TORRENT PHARMACEUTICALS LIMITED (01640547)

**Registrant**  
Torrent Pharma, Inc. (70038333)

### Establishment

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Revised: 2/2017