MOXICIP Infusion (Moxifloxacin hydrochloride)

Warning

THIS DRUG MAY CAUSE LOW BLOOD SUGAR AND MENTAL HEALTH-RELATED SIDE EFFECTS. SERIOUS ADVERSE REACTIONS CAN OCCUR, INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS and EXACERBATION OF MYASTHENIA GRAVIS

See full Prescribing Information for complete BOXED WARNING

Fluoroquinolones, including moxifloxacin, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including:
- tendinitis and tendon rupture
- peripheral neuropathy
- Central nervous system effects

Discontinue moxifloxacin injection immediately and avoid the use of fluoroquinolones, including moxifloxacin, in patients who experience any of these serious adverse reactions:
- Fluoroquinolones, including moxifloxacin, may exacerbate muscle weakness in patients with myasthenia gravis.
- Avoid moxifloxacin in patients with a known history of myasthenia gravis.

Because fluoroquinolones, including moxifloxacin, have been associated with serious adverse reactions, reserve moxifloxacin for use in patients who have no alternative treatment options for the following indications:
- Acute bacterial sinusitis
- Acute bacterial exacerbation of chronic bronchitis

Composition

Each 100 ml contains:
- Moxifloxacin Hydrochloride IP equivalent to Moxifloxacin.................400 mg
- Mannitol IP.................................................................5% w/v
- Water for Injections IP.................................................q.s.

Dosage Form

Solution for intravenous (IV) infusion.

Pharmacology

Pharmacodynamics

Mechanism of Action

Moxifloxacin is a member of the fluoroquinolone class of antibacterial agents. 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. It appears that the C8-methoxy moiety contributes to enhanced activity and lower selection of resistant mutants of Gram-positive bacteria compared to the C8-H moiety. The presence of the bulky bicycloamine substituent at the C-7 position prevents active efflux, associated with the NorA or pmrA genes seen in certain Gram-positive bacteria.

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

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

**Microbiology**
Moxifloxacin has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections:

- **Gram-positive Bacteria**
  - *Enterococcus faecalis*
  - *Staphylococcus aureus*
  - *Streptococcus anginosus*
  - *Streptococcus constellatus*
  - *Streptococcus pneumoniae* (including multidrug-resistant isolates)
  - *Streptococcus pyogenes*

*MDRSP: Multidrug-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 $\geq 2$ mcg/ml), second-generation cephalosporins (e.g. cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

- **Gram-negative Bacteria**
  - *Enterobacter cloacae*
  - *Escherichia coli*
  - *Haemophilus influenzae*
  - *Haemophilus parainfluenzae*
  - *Klebsiella pneumoniae*
  - *Moraxella catarrhalis*
  - *Proteus mirabilis*
  - *Anaerobic Bacteria*
  - *Bacteroides fragilis*
  - *Bacteroides thetaiotaomicron*
  - *Clostridium perfringens*
  - *Peptostreptococcus species*
  - *Other Microorganisms*
  - *Chlamyphilia pneumoniae*
Mycoplasma pneumoniae

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

**Gram-positive Bacteria**
- *Staphylococcus epidermidis*
- *Streptococcus agalactiae*
- *Streptococcus viridans* group

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

**Anaerobic Bacteria**
- *Fusobacterium* species
- *Prevotella* species

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**Pharmacokinetics**

**Absorption**

The mean (± standard deviation) pharmacokinetic parameters of moxifloxacin following single and multiple doses of 400 mg moxifloxacin given by 1-hour IV infusion are summarised in Table 1. The mean (± SD) elimination half-life from plasma is 12 ± 1.3 hours; steady-state is achieved after at least 3 days with a 400 mg once-daily regimen. The absolute bioavailability of moxifloxacin is approximately 90%. When switching from IV to the oral formulation, no dosage adjustment is necessary.

**Table 1: Mean (± SD) Maximum Concentration (Cmax) and Area Under The Plasma Drug Concentration-Time Curve (AUC) Values Following Single and Multiple Doses of 400 mg Moxifloxacin Given by 1-Hour IV Infusion**

<table>
<thead>
<tr>
<th></th>
<th>Cmax (mg/L)</th>
<th>AUC (mg*h/L)</th>
<th>Half-Life (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single-dose IV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy young male/female (n = 56)</td>
<td>3.9 ± 0.9</td>
<td>39.3 ± 8.6</td>
<td>8.2 to 15.4 a</td>
</tr>
<tr>
<td>Patients (n = 118)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n = 64)</td>
<td>4.4 ± 3.7</td>
<td>4.5 ± 2</td>
<td></td>
</tr>
<tr>
<td>Female (n = 54)</td>
<td>4.6 ± 4.2</td>
<td>4.3 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>&lt;65 years (n = 58)</td>
<td>4.3 ± 1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥65 years (n = 60)</td>
<td>4.6 ± 4.2</td>
<td>4.3 ± 1.3</td>
<td></td>
</tr>
<tr>
<td><strong>Multiple-dose IV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy young male (n = 8)</td>
<td>4.2 ± 0.8</td>
<td>38 ± 4.7</td>
<td>14.8 ± 2.2</td>
</tr>
<tr>
<td>Healthy elderly (n = 12; 8 male, 4 female)</td>
<td>6.1 ± 1.3</td>
<td>48.2 ± 0.9</td>
<td>10.1 ± 1.6</td>
</tr>
</tbody>
</table>
Patients \(b\) (n = 107)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n = 58)</td>
<td>4.2 ± 2.6</td>
</tr>
<tr>
<td>Female (n = 49)</td>
<td>4.6 ± 1.5</td>
</tr>
<tr>
<td>&lt;65 years (n = 52)</td>
<td>4.1 ± 1.4</td>
</tr>
<tr>
<td>≥65 years (n = 55)</td>
<td>4.7 ± 2.7</td>
</tr>
</tbody>
</table>

\(a\) Range of means from different studies

\(b\) Expected \(C_{\text{max}}\) (concentration obtained around the time of the end of the infusion)

**Distribution**

Moxifloxacin is approximately 30–50% bound to serum proteins, independent of drug concentration. The volume of distribution of moxifloxacin ranges from 1.7 to 2.7 L/kg. Moxifloxacin is widely distributed throughout the body, with tissue concentrations often exceeding plasma concentrations. Moxifloxacin 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 IV dose are summarised in Table 2. The rates of elimination of moxifloxacin from tissues generally parallel the elimination from plasma.

**Table 2: Moxifloxacin Concentrations (Mean ± SD) in Tissues and the Corresponding Plasma Concentrations After a Single 400 mg Oral or IV Dose \(a\)**

<table>
<thead>
<tr>
<th>Tissue or Fluid</th>
<th>N (number of patients)</th>
<th>Plasma Concentration (mcg/ml)</th>
<th>Tissue or Fluid Concentration (mcg/ml or mcg/g)</th>
<th>Tissue Plasma Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar macrophages</td>
<td>5</td>
<td>3.3 ± 0.7</td>
<td>61.8 ± 27.3</td>
<td>21.2 ± 10</td>
</tr>
<tr>
<td>Bronchial mucosa</td>
<td>8</td>
<td>3.3 ± 0.7</td>
<td>5.5 ± 1.3</td>
<td>1.7 ± 0.3</td>
</tr>
<tr>
<td>Epithelial lining fluid</td>
<td>5</td>
<td>3.3 ± 0.7</td>
<td>24.4 ± 14.7</td>
<td>8.7 ± 6.1</td>
</tr>
<tr>
<td><strong>Sinus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillary sinus mucosa</td>
<td>4</td>
<td>3.7 ± 1.1 (b)</td>
<td>7.6 ± 1.7</td>
<td>2 ± 0.3</td>
</tr>
<tr>
<td>Anterior ethmoid mucosa</td>
<td>3</td>
<td>3.7 ± 1.1 (b)</td>
<td>8.8 ± 4.3</td>
<td>2.2 ± 0.6</td>
</tr>
<tr>
<td>Nasal polyps</td>
<td>4</td>
<td>3.7 ± 1.1 (b)</td>
<td>9.8 ± 4.5</td>
<td>2.6 ± 0.6</td>
</tr>
<tr>
<td><strong>Skin, Musculoskeletal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blister fluid</td>
<td>5</td>
<td>3 ± 0.5 (c)</td>
<td>2.6 ± 0.9</td>
<td>0.9 ± 0.2</td>
</tr>
<tr>
<td>Subcutaneous tissue</td>
<td>6</td>
<td>2.3 ± 0.4 (d)</td>
<td>0.9 ± 0.3 (e)</td>
<td>0.4 ± 0.6</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>6</td>
<td>2.3 ± 0.4 (d)</td>
<td>0.9 ± 0.2 (e)</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td><strong>Intra-Abdominal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Metabolism

Approximately 52% of an oral or IV dose of moxifloxacin is metabolised via glucuronide and sulphate conjugation. The cytochrome (CY) P450 system is not involved in moxifloxacin metabolism, and is not affected by moxifloxacin. The sulphate conjugate (M1) accounts for approximately 38% of the dose, and is eliminated primarily in the faeces. Approximately 14% of an oral or IV dose is converted to a glucuronide conjugate (M2), which is excreted exclusively in the urine. Peak plasma concentrations of M2 are approximately 40% those of the parent drug, while plasma concentrations of M1 are generally less than 10% those of moxifloxacin. M1 and M2 are the only metabolites relevant in humans, both are microbiologically inactive. In vitro studies with CYP450 enzymes indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19 or CYP1A2, suggesting that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolised by these enzymes. There is no indication of oxidative metabolism.

### Excretion

The mean elimination half-life from plasma is 12 ± 1.3 hours; steady-state is achieved after at least 3 days with a 400 mg once-daily regimen. Approximately 45% of an oral or IV dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in faeces). A total of 96% ± 4% of an oral dose is excreted as either unchanged drug or known metabolites. The mean apparent total body clearance and renal clearance are 12 ± 2 L/hr and 2.6 ± 0.5 L/hr, respectively.

### Special Populations

#### Geriatric

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 IV infusion of 400 mg were similar to those observed in young patients.

#### Paediatric

The pharmacokinetics of moxifloxacin in paediatric subjects has not been studied.

#### Gender

There are no significant differences in moxifloxacin pharmacokinetics between male and female subjects when differences in body weight are taken into consideration. Dosage adjustments based on gender are not necessary.

#### Race

Steady-state moxifloxacin pharmacokinetics in male Japanese subjects was similar to those determined in Caucasians, following a 400 mg oral dose daily.

#### 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 haemodialysis or continuous ambulatory peritoneal dialysis (CAPD).

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>N</th>
<th>Concentration ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal tissue</td>
<td>8</td>
<td>2.9 ± 0.5</td>
</tr>
<tr>
<td>Abdominal exudate</td>
<td>10</td>
<td>2.3 ± 0.5</td>
</tr>
<tr>
<td>Abscess fluid</td>
<td>6</td>
<td>2.7 ± 0.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.6 ± 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.5 ± 1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.3 ± 1.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.6 ± 0.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.8 ± 0.4</td>
</tr>
</tbody>
</table>

*a* All moxifloxacin concentrations were measured 3 hours after a single 400 mg dose except for the abdominal tissue and exudate concentrations, which were measured at 2 hours post-dose, and the sinus concentrations, which were measured 3 hours post-dose after 5 days of dosing.

*b* N = 5

*c* N = 7

*d* N = 12

*e* Reflects only non-protein-bound concentrations of drug.
The sulphate 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.

**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.

**Photosensitivity Potential**

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. It is difficult to ascribe relative photosensitivity/phototoxicity among various fluoroquinolones during actual patient use because other factors play a role in determining a subject’s susceptibility to this adverse event such as a patient’s skin pigmentation, frequency and duration of sun and artificial UV light exposure, wearing of sunscreen and protective clothing, the use of other concomitant drugs, and the dosage and duration of fluoroquinolone therapy.

**Indications**

MOXICIP IV is indicated for the treatment of adults (≥18 years of age) with infections caused by susceptible isolates of the designated microorganisms in the conditions listed below:

- **Community-acquired Pneumonia** caused by *Streptococcus pneumoniae* (including multi-drug resistant isolates*), *Haemophilus influenzae*, *Moraxella catarrhalis*, methicillin-susceptible *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Mycoplasma pneumoniae*, or *Chlamydia pneumoniae*.
*MDRSP: Multidrug-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 (minimum inhibitory concentrations ≥2 mcg/ml), second-generation cephalosporins (e.g. cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

- **Uncomplicated Skin and Skin Structure Infections** caused by methicillin-susceptible *Staphylococcus aureus* or *Streptococcus pyogenes*.

- **Acute Bacterial Sinusitis** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*.
Because fluoroquinolones, including moxifloxacin injection, have been associated with serious adverse reactions and, for some patients, acute bacterial sinusitis is self-limiting, reserve moxifloxacin injection for the treatment of acute bacterial sinusitis in patients who have no alternative treatment options.

- **Acute Bacterial Exacerbation of Chronic Bronchitis (ABECB)** caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Klebsiella pneumoniae*, methicillin-susceptible *Staphylococcus aureus*, or *Moraxella catarrhalis*.
Because fluoroquinolones, including moxifloxacin injection, have been associated with serious adverse reactions and, for some patients, ABECB is self-limiting, reserve moxifloxacin injection for the treatment of ABECB in patients who have no alternative treatment options.

**Usage**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of moxifloxacin injection and other antibacterial drugs, moxifloxacin injection 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.
Culture and Susceptibility Testing
Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to moxifloxacin. Therapy with moxifloxacin injection may be initiated before results of these tests are known; once the results become available, appropriate therapy should be continued.

Dosage And Administration

Dosage

Adults
The dose of moxifloxacin injection is 400 mg by the IV route once every 24 hours. The duration of therapy depends on the type of infection, as described in Table 3.

Table 3: Dosage and Duration of Therapy in Adult Patients

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Dose Every 24 hours</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired pneumonia</td>
<td>400 mg</td>
<td>7–14 days</td>
</tr>
<tr>
<td>Uncomplicated Skin and Skin Structure Infections</td>
<td>400 mg</td>
<td>7 days</td>
</tr>
<tr>
<td>Acute Bacterial Sinusitis</td>
<td>400 mg</td>
<td>10 days</td>
</tr>
<tr>
<td>Acute Bacterial Exacerbation of Chronic Bronchitis</td>
<td>400 mg</td>
<td>5 days</td>
</tr>
</tbody>
</table>

Note:

* Due to the designated pathogens (refer to INDICATIONS section).

b Sequential therapy (IV to oral) may be instituted at the discretion of the physician.

When switching from IV to oral dosage administration, no dosage adjustment is necessary. Patients whose therapy is started with moxifloxacin injection may be switched to moxifloxacin tablets when clinically indicated at the discretion of the physician.

Method of Administration

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.
Moxifloxacin injection should be administered by IV infusion only. It is not intended for intra-arterial, intramuscular, intrathecal, intraperitoneal or subcutaneous administration.
Moxifloxacin injection should be administered by IV infusion over a period of 60 minutes by direct infusion or through a Y-type IV infusion set that may already be in place.
Caution: Rapid or bolus IV infusion must be avoided.
Because only limited data are available on the compatibility of moxifloxacin IV injection with other IV substances, additives or other medications should not be added to moxifloxacin injection or infused simultaneously through the same IV line. If the same IV line or a Y-type line is used for sequential infusion of other drugs or if the 'piggyback' method of


administration is used, the line should be flushed before and after infusion of moxifloxacin injection with an infusion solution compatible with moxifloxacin injection as well as with other drug(s) administered via this common line. Moxifloxacin injection is compatible with the following IV solutions at ratios from 1:10 to 10:1 as mentioned in Table 4.

Table 4: Compatible IV Solutions for Moxifloxacin Injection

<table>
<thead>
<tr>
<th>Solution</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% Sodium Chloride Injection, USP</td>
<td>Sterile Water for Injection, USP</td>
</tr>
<tr>
<td>1M Sodium Chloride Injection</td>
<td>10% Dextrose for Injection, USP</td>
</tr>
<tr>
<td>5% Dextrose Injection, USP</td>
<td>Lactated Ringer's for Injection</td>
</tr>
</tbody>
</table>

**Special Populations**

**Paediatric**
The pharmacokinetics of moxifloxacin in paediatric subjects has not been studied. Safety and effectiveness in paediatric patients and adolescents <18 years of age have not been established.

**Geriatric**
No dosage adjustment is necessary based on age. The clinical trial data demonstrate that the safety of IV moxifloxacin in patients aged ≥65 years was similar to that of comparator-treated patients.

**Renal Impairment**
The pharmacokinetic parameters of moxifloxacin are not significantly altered in mild, moderate, severe or end-stage renal disease. No dosage adjustment is required in renally impaired patients, including those on either haemodialysis or CAPD.

**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.

**Contraindications**

Moxifloxacin is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antimicrobial agents.

**Warnings And Precautions**

**General**
The drug may cause low blood sugar and mental health-related side effects. Low blood sugar levels, also called hypoglycaemia, can lead to coma. The mental health side effects are more prominent and more consistent across the systemic fluoroquinolone drug class.

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

Fluoroquinolones, including moxifloxacin injection, have been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system (CNS) effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions
can occur within hours to weeks after starting moxifloxacin. Patients of any age or without pre-existing risk factors have experienced these adverse reactions. Discontinue moxifloxacin injection immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including moxifloxacin, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.

**Tendinitis and Tendon Rupture**

Fluoroquinolones, including moxifloxacin, are associated with an increased risk of tendinitis and tendon rupture in all ages. 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 further increased in patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Other factors that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendinitis and tendon rupture have also occurred in patients taking fluoroquinolones who do not have the above risk factors. Discontinue moxifloxacin if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug. Avoid fluoroquinolones, including moxifloxacin, in patients who have a history of tendon disorders or have experienced tendinitis or tendon rupture.

**Peripheral Neuropathy**

Fluoroquinolones, including moxifloxacin, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting the small and/or large axons and resulting in paresthesias, hypoesthesias, dyesthesias and weakness have been reported in patients receiving fluoroquinolones, including moxifloxacin. Symptoms may occur soon after initiation of moxifloxacin and may be irreversible in some patients.

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

Patients under treatment with moxifloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy develop in order to prevent the development of an irreversible condition.

**CNS Effects**

Fluoroquinolones, including moxifloxacin, have been associated with increased risk of CNS reactions, including convulsions and increased intracranial pressure (including pseudotumour cerebri), and toxic psychosis. Fluoroquinolones may also cause CNS reactions of nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression and, rarely, suicidal thoughts or acts.

These reactions may occur following the first dose. If these reactions occur in patients receiving moxifloxacin, discontinue moxifloxacin immediately and institute appropriate measures. As with all fluoroquinolones, moxifloxacin should be used with caution in patients with known or suspected CNS disorders (e.g. severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold. In case of seizures, treatment with moxifloxacin should be discontinued and appropriate measures instituted.

**Exacerbation of Myasthenia Gravis**

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

QT Prolongation
Moxifloxacin has been shown to prolong the QT interval of the electrocardiogram (ECG) in some patients. The drug should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia and patients receiving Class IA (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) anti-arrhythmic agents, due to the lack of clinical experience with the drug in these patient populations.

Pharmacokinetic studies between moxifloxacin and other drugs that prolong the QT interval such as cisapride, erythromycin, antipsychotics and tricyclic antidepressants have not been performed. An additive effect of moxifloxacin and these drugs cannot be excluded; therefore, caution should be exercised when moxifloxacin is given concurrently with these drugs. In premarketing clinical trials, the rate of cardiovascular adverse events was similar in 798 moxifloxacin- and 702 comparator-treated patients who received concomitant therapy with drugs known to prolong the QTc interval.

Moxifloxacin should be used with caution in patients who are taking medications that can reduce potassium levels. Moxifloxacin should be used with caution in patients who are taking medications associated with clinically significant bradycardia.

Moxifloxacin should be used with caution in patients with ongoing pro-arrhythmic conditions, such as clinically significant bradycardia, acute myocardial ischaemia. The magnitude of QT prolongation may increase with increasing concentrations of the drug or increasing rates of infusion of the IV formulation. Therefore, the recommended dose or infusion rate should not be exceeded. QT prolongation may lead to an increased risk for ventricular arrhythmias, including torsades de pointes. Treatment with moxifloxacin should be stopped if signs or symptoms that may be associated with cardiac arrhythmia occur during treatment, with or without ECG findings. No excess in cardiovascular morbidity or mortality attributable to QTc prolongation occurred with moxifloxacin treatment in over 15,500 patients in controlled clinical studies, including 759 patients who were hypokalemic at the start of treatment, and there was no increase in mortality in over 18,000 moxifloxacin tablet-treated patients in a postmarketing observational study in which ECGs were not performed. Female patients and elderly patients using moxifloxacin may be more susceptible to drug-associated QT prolongation. In addition, moxifloxacin should be used with caution in patients with mild, moderate or severe liver cirrhosis.

Hypersensitivity Reactions
Serious anaphylactic reactions, some following the first dose, have been reported in patients receiving fluoroquinolone therapy, including moxifloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnoea, urticaria, and itching. Discontinue moxifloxacin injection at the first appearance of a skin rash or any other sign of hypersensitivity.

Other Serious, and Sometimes Fatal, Adverse Reactions
Other serious, and sometimes fatal, events, some due to hypersensitivity and some due to uncertain etiology, have been reported rarely in patients receiving therapy with quinolones, including moxifloxacin. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following:

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

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

C. difficile-associated Diarrhoea

Clostridium difficile-associated diarrhoea (CDAD) has been reported with the use of nearly all antibacterial agents, including moxifloxacin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, leading to overgrowth of C. difficile.

C. difficile produces toxins A and B, which contribute to the development of CDAD. Hypertoxin-producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over 2 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.

Arthropathic Effects on Animals

The oral administration of moxifloxacin caused lameness in immature dogs. Histopathological examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage. Related quinolone-class drugs also produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species.

Blood Glucose Disturbances

As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycaemia (low blood sugar levels) and hyperglycaemia have been reported with moxifloxacin. In moxifloxacin-treated patients, dysglycaemia occurred predominantly in elderly diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. sulphonylurea) or with insulin. In diabetic patients, careful monitoring of blood glucose is recommended. If a hypoglycaemic reaction occurs, moxifloxacin should be discontinued and appropriate therapy should be initiated immediately. Hypoglycaemia can lead to coma.

Photosensitivity/Phototoxicity

Moderate-to-severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g. burning, erythema, exudation, vesicles, blistering, oedema) 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 quinolone antibiotics after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if phototoxicity occurs.

Development of Drug-resistant Bacteria

Prescribing moxifloxacin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Severe Liver Disorders

Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with moxifloxacin. Patients should be advised to contact their doctor prior to continuing treatment if signs and symptoms of fulminant hepatic disease develop such as rapidly developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy.

Liver function tests/investigations should be performed in cases where indications of liver dysfunction occur.

Vision Disorders

If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.
**Patients with Glucose-6-Phosphate Dehydrogenase Deficiency**
Patients with a family history of or actual glucose-6-phosphate dehydrogenase deficiency are prone to haemolytic reactions when treated with quinolones. Therefore, moxifloxacin should be used with caution in these patients.

**Peri-Arterial Tissue Inflammation**
Moxifloxacin solution for infusion is for IV administration only. Intra-arterial administration should be avoided since preclinical studies demonstrated peri-arterial tissue inflammation following infusion by this route.

**Patients with Special Complicated Skin and Skin Structure Infections**
Clinical efficacy of moxifloxacin in the treatment of severe burn infections, fasciitis and diabetic foot infections with osteomyelitis has not been established.

**Interference with Biological Tests**
Moxifloxacin therapy may interfere with the *Mycobacterium* species culture test by suppression of mycobacterial growth, causing false-negative results in samples taken from patients currently receiving moxifloxacin.

**Patients with Methicillin-resistant Staphylococcus aureus (MRSA) Infections**
Moxifloxacin is not recommended for the treatment of MRSA infections. In case of a suspected or confirmed infection due to MRSA, treatment with an appropriate antibacterial agent should be started.

### Drug Interactions

**Antacids, Sucralfate, Multivitamins, and products containing other Multivalent Cations:**
Quinolones form chelates with alkaline earth and transition metal cations. Oral administration of quinolones with antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, or with formulations containing divalent and trivalent cations such as didanosine chewable/buffered tablets or the pediatric powder for oral solution, may substantially interfere with the absorption of quinolones, resulting in systemic concentrations considerably lower than desired. Therefore, moxifloxacin should be taken at least 4 hours before or 8 hours after these agents.

**Warfarin**
Quinolones, including moxifloxacin, 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 (PT), International Normalised Ratio (INR), or other suitable anticoagulation tests should be closely monitored if a quinolone is administered concomitantly with warfarin or its derivatives.

**Antidiabetic Agents**
Disturbances of blood glucose, including hyperglycaemia and hypoglycaemia, have been reported in patients treated concomitantly with fluoroquinolones and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered. If a hypoglycaemic reaction occurs, moxifloxacin should be discontinued and appropriate therapy should be initiated immediately.

**Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)**
Although not observed with moxifloxacin in preclinical and clinical trials, the concomitant administration of a NSAID with a quinolone may increase the risks of CNS stimulation and convulsions.

**Drugs that Prolong QT**
There is limited information available on the potential for a pharmacodynamic interaction in humans between moxifloxacin and other drugs that prolong the QTc interval of the ECG. Sotalol, a Class III anti-arrhythmic, has been shown to further increase the QTc interval when combined with high doses of IV moxifloxacin in dogs. Therefore, moxifloxacin should be avoided with Class IA and Class III anti-arrhythmics.

**Others**
Moxifloxacin should be used with caution in patients who are taking medications that can reduce potassium levels (e.g.[
loop and thiazide-type diuretics, laxatives and enemas, corticosteroids, amphotericin B) or medication that is associated with clinically significant bradycardia.

Renal Impairment

See under DOSAGE AND ADMINISTRATION.

Hepatic Impairment

See under DOSAGE AND ADMINISTRATION.

Pregnancy

Pregnancy Category C. Since there are no adequate or well-controlled studies in pregnant women, moxifloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Fertility

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), or at IV 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 oestrous cycle in female rats.

Lactation

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

Pediatric Use

Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. Moxifloxacin causes arthropathy in juvenile animals.

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. This risk is further increased in patients receiving concomitant corticosteroid therapy. Tendinitis or tendon rupture can involve the Achilles, hand, shoulder, or other tendon sites and can occur during or after completion of therapy; cases occurring up to several months after fluoroquinolone treatment have been reported. Caution should be used when prescribing moxifloxacin injection to elderly patients, especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue moxifloxacin injection and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur.

In general, elderly patients may be more susceptible to drug-associated effects of the QT interval. Therefore, moxifloxacin injection should be avoided in patients taking drugs that can result in prolongation of the QT interval (e.g. class IA or class III anti-arrhythmics) or in patients with risk factors for torsades de pointes (e.g. known QT prolongation, uncorrected hypokalemia).

Effects on Ability to Drive and Use Machines

No studies on the effects of moxifloxacin on the ability to drive and use machines have been performed. However, fluoroquinolones including moxifloxacin may result in an impairment of the patient's ability to drive or operate machinery due to CNS reactions (e.g. dizziness; acute, transient loss of vision) or acute and short lasting loss of
consciousness (syncope). Patients should be advised to see how they react to moxifloxacin before driving or operating machinery.

Undesirable Effects

Consciousness (syncope). Patients should be advised to see how they react to moxifloxacin before driving or operating machinery.

Undesirable Effects

Undesirable Effects

The following serious and otherwise important adverse reactions are discussed in the WARNINGS AND PRECAUTIONS section:

Disabling and Potentially Irreversible Serious Adverse Reactions, Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and CNS Effects

Tendinitis and Tendon Rupture

Peripheral Neuropathy

CNS Effects

Exacerbation of Myasthenia Gravis

QT Prolongation

Hypersensitivity Reactions

Other Serious, and Sometimes Fatal, Adverse Reactions

Clostridium difficile-Associated Diarrhoea

Blood Glucose Disturbances

Photosensitivity/Phototoxicity

Development of Drug-resistant Bacteria

Clinical Trial 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 in 14,981 patients in 71 active controlled Phase II–IV clinical trials in different indications. The population studied had a mean age of 50 years (approximately 73% of the population was <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, IV, or sequentially (IV followed by oral). Treatment duration was usually 6–10 days, and the mean number of days on therapy was 9 days.

Discontinuation of moxifloxacin due to adverse events occurred in 5% of patients overall, 4.1% of patients treated with 400 mg oral, 3.9% with 400 mg IV, and 8.2% with sequential therapy 400 mg oral/IV. The most common adverse events leading to discontinuation with the 400 mg oral doses were nausea (0.8%), diarrhoea (0.5%), dizziness (0.5%), and vomiting (0.4%). The most common adverse event leading to discontinuation with the 400 mg IV dose was rash (0.5%). The most common adverse events leading to discontinuation with the 400 mg IV/oral sequential dose were diarrhoea (0.5%) and pyrexia (0.4%).

Adverse reactions occurring in ≥1% of moxifloxacin-treated patients and less common adverse reactions, occurring in 0.1 to <1% of moxifloxacin-treated patients are shown in Table 5 and Table 6, respectively. The most common adverse drug reactions (≥3%) were nausea, diarrhoea, headache, and dizziness.

Table 5: Common (≥1%) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin
<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>Anemia</td>
<td>1.1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea</td>
<td>6.9</td>
</tr>
<tr>
<td></td>
<td>Diarrhoea</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain upper</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia</td>
<td>1.0</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Pyrexia</td>
<td>1.1</td>
</tr>
<tr>
<td>Investigations</td>
<td>Alanine aminotransferase increased</td>
<td>1.1</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>4.2</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>3.0</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>Insomnia</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Table 6: Less Common (0.1 to <1%) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin (N = 14,981)
| Gastrointestinal Disorders | Dry mouth  
| | Abdominal discomfort  
| | Flatulence  
| | Abdominal distention  
| | Gastritis  
| | Gastro-oesophageal reflux disease  
| General Disorders and Administration Site Conditions | Fatigue  
| | Chest pain  
| | Asthenia  
| | Oedema peripheral  
| | Pain  
| | Malaise  
| | Infusion-site extravasation  
| | Oedema  
| | Chills  
| | Chest discomfort  
| | Facial pain  
| Hepatobiliary Disorders | Hepatic function abnormal  
| Infections and Infestations | Vulvovaginal candidiasis  
| | Oral candidiasis  
| | Vulvovaginal mycotic infection  
| | Candidiasis  
| | Vaginal infection  
| | Oral fungal infection  
| | Fungal infection  
| | Gastroenteritis  

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Aspartate aminotransferase increased</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gamma-glutamyl transferase increased</td>
</tr>
<tr>
<td></td>
<td>Blood alkaline phosphatase increased</td>
</tr>
<tr>
<td></td>
<td>Hepatic enzyme increased</td>
</tr>
<tr>
<td></td>
<td>ECG QT prolonged</td>
</tr>
<tr>
<td></td>
<td>Blood lactate dehydrogenase increased</td>
</tr>
<tr>
<td></td>
<td>Platelet count increased</td>
</tr>
<tr>
<td></td>
<td>Blood amylase increased</td>
</tr>
<tr>
<td></td>
<td>Blood glucose increased</td>
</tr>
<tr>
<td></td>
<td>Lipase increased</td>
</tr>
<tr>
<td></td>
<td>Haemoglobin decreased</td>
</tr>
<tr>
<td></td>
<td>Blood creatinine increased</td>
</tr>
<tr>
<td></td>
<td>Transaminases increased</td>
</tr>
<tr>
<td></td>
<td>White blood cell count increased</td>
</tr>
<tr>
<td></td>
<td>Blood urea increased</td>
</tr>
<tr>
<td></td>
<td>Liver function test abnormal</td>
</tr>
<tr>
<td></td>
<td>Haematocrit decreased</td>
</tr>
<tr>
<td></td>
<td>Prothrombin time prolonged</td>
</tr>
<tr>
<td></td>
<td>Eosinophil count increased</td>
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<tr>
<td></td>
<td>Activated partial thromboplastin time</td>
</tr>
<tr>
<td></td>
<td>prolonged</td>
</tr>
<tr>
<td></td>
<td>Blood bilirubin increased</td>
</tr>
<tr>
<td></td>
<td>Blood triglycerides increased</td>
</tr>
<tr>
<td></td>
<td>Blood uric acid increased</td>
</tr>
<tr>
<td></td>
<td>Blood pressure increased</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td>Hyperglycaemia</td>
</tr>
<tr>
<td></td>
<td>Anorexia</td>
</tr>
<tr>
<td></td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td>Decreased appetite</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>Back pain</td>
</tr>
<tr>
<td></td>
<td>Pain in extremity</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
</tr>
<tr>
<td></td>
<td>Muscle spasms</td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal chest pain</td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal pain</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Dysgeusia</td>
</tr>
<tr>
<td></td>
<td>Somnolence</td>
</tr>
<tr>
<td></td>
<td>Tremor</td>
</tr>
<tr>
<td></td>
<td>Lethargy</td>
</tr>
<tr>
<td></td>
<td>Paresthesia</td>
</tr>
<tr>
<td></td>
<td>Tension headache</td>
</tr>
<tr>
<td></td>
<td>Hypoesthesia</td>
</tr>
<tr>
<td></td>
<td>Syncope</td>
</tr>
</tbody>
</table>
| Psychiatric Disorders | Anxiety  
|----------------------|---------  
|                      | Confusional state  
|                      | Agitation  
|                      | Depression  
|                      | Nervousness  
|                      | Restlessness  
|                      | Hallucination  
|                      | Disorientation  
| Renal and Urinary Disorders | Renal failure  
|                        | Dysuria  
|                        | Renal failure acute  
| Reproductive System and Breast Disorders | Vulvovaginal pruritus  
| Respiratory, Thoracic and Mediastinal Disorders | Dyspnoea  
|                        | Asthma  
|                        | Wheezing  
|                        | Bronchospasm  
| Skin and Subcutaneous Tissue Disorders | Rash  
|                        | Pruritus  
|                        | Hyperhidrosis  
|                        | Erythema  
|                        | Urticaria  
|                        | Dermatitis allergic  
|                        | Night sweats  
| Vascular Disorders | Hypertension  
|                      | Hypotension  
|                      | Phlebitis  

### Mental Side Effects

The mental side effects that are more prominent and more consistent across the systemic fluoroquinolone drug class are as follows:
- Disturbances in attention
- Disorientation
- Agitation
- Nervousness
- Memory Impairment
- Serious disturbances in mental abilities called delirium

### Laboratory Changes

Changes in laboratory parameters, without regard to drug relationship, which are not listed above and which occurred in ≥2% of patients and at an incidence greater than in controls included: increases in mean corpuscular haemoglobin (MCH), neutrophils, white blood cells (WBCs), PT ratio, ionised calcium, chloride, albumin, globulin, bilirubin; decreases in haemoglobin, red blood cells (RBCs), neutrophils, eosinophils, basophils, PT ratio, glucose, partial pressure of oxygen (pO₂), bilirubin and amylase. It cannot be determined if any of the above laboratory abnormalities were caused by the drug or the underlying condition being treated.
Below is the list of adverse reactions that have been identified during post-approval use of moxifloxacin. 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 7: Postmarketing Reports of Adverse Drug Reactions**

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Agranulocytosis</td>
</tr>
<tr>
<td></td>
<td>Pancytopenia</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Ventricular tachyarrhythmias (including, in very rare cases, cardiac arrest and torsades de pointes, and usually in patients with concurrent severe underlying pro-arhythmic conditions)</td>
</tr>
<tr>
<td>Ear and Labyrinth Disorders</td>
<td>Hearing impairment, including deafness (reversible in majority of cases)</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>Vision loss (especially in the course of CNS reactions, transient in majority of cases)</td>
</tr>
<tr>
<td>Hepatobiliary Disorders</td>
<td>Hepatitis (predominantly cholestatic)</td>
</tr>
<tr>
<td></td>
<td>Hepatic failure (including fatal cases)</td>
</tr>
<tr>
<td></td>
<td>Jaundice</td>
</tr>
<tr>
<td></td>
<td>Acute hepatic necrosis</td>
</tr>
<tr>
<td>Immune System Disorders</td>
<td>Anaphylactic reaction</td>
</tr>
<tr>
<td></td>
<td>Anaphylactic shock</td>
</tr>
<tr>
<td></td>
<td>Angio-oedema (including laryngeal oedema)</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>Tendon rupture</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Altered coordination</td>
</tr>
<tr>
<td></td>
<td>Abnormal gait</td>
</tr>
<tr>
<td></td>
<td>Myasthenia gravis (exacerbation of)</td>
</tr>
<tr>
<td></td>
<td>Muscle weakness</td>
</tr>
<tr>
<td></td>
<td>Peripheral neuropathy (that may be irreversible), polyneuropathy</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>Psychotic reaction (very rarely culminating in self-injurious behaviour, such as suicidal ideation/thoughts or suicide attempts)</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td></td>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>Allergic pneumonitis</td>
</tr>
</tbody>
</table>
### Skin and Subcutaneous Tissue Disorders
- Photosensitivity/phototoxicity reaction
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis

### Other Undesirable Effects

Few other adverse reactions observed in clinical trials and derived from post-marketing reports with moxifloxacin 400 mg daily administered by the IV or oral route (IV only, sequential and oral administration) sorted by frequencies are listed below:

Apart from nausea and diarrhoea, all adverse reactions were observed at frequencies below 3%.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Frequencies are defined as:
- common (≥1/100 to <1/10);
- uncommon (≥1/1,000 to <1/100);
- rare (≥1/10,000 to <1/1,000); and,
- very rare (<1/10,000)

### Infections and Infestations
Common: superinfections due to resistant bacteria or fungi, e.g. oral and vaginal candidiasis.

### Metabolism and Nutrition Disorders
Rare: hyperuricaemia

### Psychiatric Disorders
Uncommon: psychomotor hyperactivity
Rare: emotional lability
Very Rare: depersonalisation

### Nervous System Disorders
Uncommon: paresthesia and dysesthesia, taste disorders (including ageusia in very rare cases)
Rare: smell disorders (including anosmia), abnormal dreams, disturbed attention, seizures including grand mal convulsions, speech disorders, amnesia
Very Rare: hyperesthesia

### Eye Disorders
Uncommon: visual disturbances, including diplopia
Rare: photophobia
Very Rare: uveitis and bilateral acute iris transillumination

### Cardiac Disorders
Common: QT prolongation in patients with hypokalemia
Uncommon: QT prolongation

### Vascular Disorders
Uncommon: vasodilatation
Very Rare: vasculitis

### Gastrointestinal Disorders
Rare: dysphagia, stomatitis, antibiotic-associated colitis (including pseudo-membranous colitis, in very rare cases associated with life-threatening complications)

### Skin and Subcutaneous Tissue Disorders
Uncommon: dry skin

### Musculoskeletal and Connective Tissue Disorders
Rare: tendonitis, muscle cramp, muscle twitching
Very Rare: arthritis, muscle rigidity

**General Disorders and Administration Site Conditions**

Common: injection and infusion-site reactions
Uncommon: painful conditions (including pain in back, chest, pelvic and extremities), sweating, infusion site (thrombo-) phlebitis

**Hepatobiliary Disorders**

Very Rare: fulminant hepatitis potentially leading to life-threatening liver failure (including fatal cases)

The following undesirable effects have a higher frequency category in the subgroup of IV-treated patients with or without subsequent oral therapy:

Common: increased gamma-glutamyl-transferase
Uncommon: ventricular tachyarrhythmias, hypotension, oedema, antibiotic-associated colitis (including pseudomembranous colitis), in very rare cases associated with life-threatening complications, seizures, including grand mal convulsions, hallucination, renal impairment (including increase in blood urea nitrogen and creatinine), renal failure.

There have been very rare cases of the following side effects reported following treatment with other fluoroquinolones, which might possibly also occur during treatment with moxifloxacin: increased intracranial pressure (including pseudotumour cerebri), hypernatremia, hypercalcemia, haemolytic anemia, rhabdomyolysis, photosensitivity reactions.

If you experience any side effects, talk to your doctor or pharmacist or write to drugsafety@Cipla.com. You can also report side effects directly via the National Pharmacovigilance Programme of India by calling on 1800 180 3024. By reporting side effects, you can help provide more information on the safety of this product.

### Overdosage

Single oral overdoses up to 2.8 g were not associated with any serious adverse events. In the event of acute overdose, the stomach should be emptied and adequate hydration maintained. ECG monitoring is recommended due to the possibility of QT interval prolongation. The patient should be carefully observed and given supportive treatment. The administration of activated charcoal as soon as possible after oral overdose may prevent excessive increase of systemic moxifloxacin exposure. About 3% and 9% of the dose of moxifloxacin, as well as about 2% and 4.5% of its glucuronide metabolite, are removed by CAPD and haemodialysis, respectively.

### Incompatibility

The following solutions are incompatible with moxifloxacin solution for infusion:
- Sodium chloride 10% and 20% solutions
- Sodium bicarbonate 4.2% and 8.4% solutions

This medicinal product must not be mixed with other medicinal products except those mentioned in the section DOSAGE AND ADMINISTRATION.

### Storage And Handling Instructions

Parenteral drug products should be inspected visually for particulate matter prior to administration. Samples containing visible particulates should not be used.
Store in a cool place. Protect from light. Do not freeze.
Packaging Information

MOXICIP Infusion: Bottle of 100 ml.
Last Reviewed: July 2019
Last Updated: July 2019

MOXICIP Infusion

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