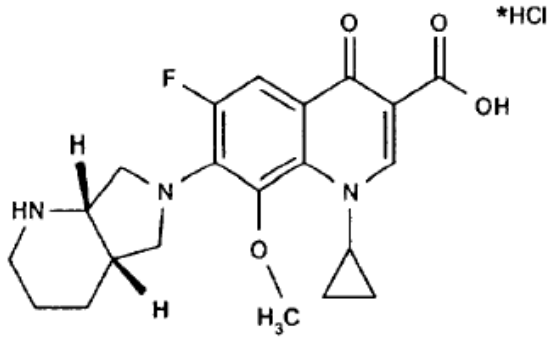
For the use only of a Registered Medical Practitioner only

MOXIF I.V.
(Moxifloxacin Intravenous Infusion)

COMPOSITION
Moxifloxacin Intravenous Infusion
Each 100ml infusion contains
Moxifloxacin Hydrochloride B.P. equivalent to Moxifloxacin 400 mg
Mannitol I.P. 5% W/V
Water for Injection I. P. q.s.

DESCRIPTION
Moxifloxacin Hydrochloride is a syenthetic broad spectrum antibacterial agent for oral administration. Moxifloxacin , a fluoroquinolone, is available as the monohydrochloride salt of 1 cyclopropyl-7-[(s,s)-2-8-diazabicyclo[4.3.0]non-8-y1]-6-fluro-8-methoxy-1,4- dihydro-4-oxo-3 quinolinecarboxylic acid, it is a slightly yellow to yellow crystalline Substance with a molecular weight of 437.9.its empirical formula is $C_{21}H_{24}FN_3O_4$.HCl. The chemical structure is as follows:



CLINICAL PHARMACOLOGY
PHARMACODYNAMICS
Mechanism of action
Moxifloxacin has in vitro activity against a wide range of Gram-positive and Gram-negative pathogens. The bactericidal action of moxifloxacin results from the inhibition of both type II topoisomerases (DNA gyrase and topoisomerase IV) required for bacterial DNA replication, transcription and repair. 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.

Pharmacodynamic investigations have demonstrated that moxifloxacin exhibits a concentration dependent killing rate. Minimum bactericidal concentrations (MBC) were found to be in the range of the minimum inhibitory concentrations (MIC). Interference with culture test Moxifloxacin therapy may give false negative culture results for Mycobacterium spp. by suppression of mycobacterial growth.

Effect on the intestinal flora in humans
The following changes in the intestinal flora were seen in volunteers following oral administration of moxifloxacin: Escherichia coli, Bacillus spp., Enterococcus spp., and Klebsiella spp. were reduced, as were the anaerobes Bacteroides vulgatus, Bifidobacterium spp., Eubacterium spp., and Peptostreptococcus spp.. For Bacteroides fragilis there was an increase. These changes returned to normal within two weeks.

Mechanism of resistance
Resistance mechanisms that inactivate penicillins, cephalosporins, aminoglycosides, macrolides and tetracyclines do not interfere with the antibacterial activity of moxifloxacin. Other resistance mechanisms such as permeation barriers (common in Pseudomonas aeruginosa) and efflux mechanisms may also effect susceptibility to moxifloxacin.

In vitro resistance to moxifloxacin is acquired through a stepwise process by target site mutations in type II topoisomerases, DNA gyrase and topoisomerase IV. Moxifloxacin is a poor substrate for active efflux mechanisms in Gram-positive organisms.

Cross-resistance is observed with other fluoroquinolones. However, as moxifloxacin inhibits both topoisomerase II and IV with similar activity in some Gram-positive bacteria, such bacteria may be resistant to other quinolones, but susceptible to moxifloxacin.

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 significantly affect the extent or rate of systemic absorption (AUC).

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

	C_{max} (mg/L)	AUC (mg•h/L)	Half-life (hr)
Single Dose Oral Healthy (n = 372)	3.1 ± 1	36.1 ± 9.1	11.5 - 15.6[a]
Multiple Dose Oral			
Healthy young male/female (n = 15)	4.5 ± 0.5	48 ± 2.7	12.7 ± 1.9
Healthy elderly male (n = 8)	3.8 ± 0.3	51.8 ± 6.7	
Healthy elderly female (n = 8)	4.6 ± 0.6	54.6 ± 6.7	
Healthy young male (n = 8)	3.6 ± 0.5	48.2 ± 9	
Healthy young female (n = 9)	4.2 ± 0.5	49.3 ± 9.5	

a) Range of means from different studies

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

	C_{max} (mg/L)	AUC (mg•h/L)	Half-life (hr)
Single Dose IV			
Healthy young male/female (n = 56)	3.9 ± 0.9	39.3 ± 8.6	8.2 - 15.4[a]
Patients (n = 118)			
Male (n = 64)	4.4 ± 3.7		
Female (n = 54)	4.5 ± 2		
< 65 years (n = 58)	4.6 ± 4.2		
≥ 65 years (n = 60)	4.3 ± 1.3		
Multiple Dose IV			
Healthy young male (n = 8)	4.2 ± 0.8	38 ± 4.7	14.8 ± 2.2
Healthy elderly (n =12; 8 male, 4 female)	6.1 ± 1.3	48.2 ± 0.9	10.1 ± 1.6
Patients[b] (n = 107)			
Male (n = 58)	4.2 ± 2.6		
Female (n = 49)	4.6 ± 1.5		
<65 years (n = 52)	4.1 ± 1.4		
≥65 years (n = 55)	4.7 ± 2.7		

a) Range of means from different studies

b) Expected C_{max} (concentration obtained around the time of the end of the infusion) Plasma concentrations increase proportionately 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.

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 summarized in Table. The rates of elimination of moxifloxacin from tissues generally parallel the elimination from plasma.

Table: Moxifloxacin Concentrations (mean ± SD) in Tissues and the Corresponding Plasma Concentrations after a Single 400 mg Oral or Intravenous Dose[a]

Tissue or Fluid	N	Plasma Concentration (mcg/mL)	Tissue or Fluid Concentration (mcg/mL or mcg/g)	Tissue Plasma Ratio
Respiratory				
Alveolar Macrophages	5	3.3 ± 0.7	61.8 ± 27.3	21.2 ± 10
Bronchial Mucosa	8	3.3 ± 0.7	5.5 ± 1.3	1.7 ± 0.3

Epithelial Lining Fluid	5	3.3 ± 0.7	24.4 ± 14.7	8.7 ± 6.1
Sinus				
Maxillary Sinus Mucosa	4	3.7 ± 1.1b	7.6 ± 1.7	2 ± 0.3
Anterior Ethmoid Mucosa	3	3.7 ± 1.1b	8.8 ± 4.3	2.2 ± 0.6
Nasal Polyps	4	3.7 ± 1.1b	9.8 ± 4.5	2.6 ± 0.6
Skin, Musculoskeletal				
Blister Fluid	5	3 ± 0.5c	2.6 ± 0.9	0.9 ± 0.2
Subcutaneous Tissue	6	2.3 ± 0.4d	0.9 ± 0.3e	0.4 ± 0.6
Skeletal Muscle	6	2.3 ± 0.4d	0.9 ± 0.2e	0.4 ± 0.1
Intra-Abdominal				
Abdominal tissue	8	2.9 ± 0.5	7.6 ± 2	2.7 ± 0.8
Abdominal exudates	10	2.3 ± 0.5	3.5 ±1.2	1.6 ± 0.7
Abscess fluid	6	2.7 ± 0.7	2.3 ±1.5	0.8±0.4

a) All moxifloxacin concentrations were measured 3 hours after a single 400 mg dose, except the abdominal tissue and exudates 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.

Metabolism
Approximately 52% of an oral or intravenous dose of moxifloxacin is metabolized via glucuronide and sulfate conjugation. The cytochrome P450 system is not involved in moxifloxacin metabolism, and is not affected by moxifloxacin. The sulfate conjugate (M1) accounts for approximately 38% of the dose, and is eliminated primarily in the feces. Approximately 14% of an oral or intravenous 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.

In vitro studies with cytochrome (CYP) P450 enzymes indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2, suggesting that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these enzymes.

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 96% ± 4% of an oral dose is excreted as either unchanged drug or known metabolites. The mean (± SD) apparent total body clearance and renal clearance are 12 ± 2 L/hr and 2.6 ± 0.5 L/hr, respectively.

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.

Pediatric
The pharmacokinetics of moxifloxacin in pediatric subjects has not been studied.

Gender
Following oral administration of 400 mg moxifloxacin daily for 10 days to 23 healthy males (19-75 years) and 24 healthy females (19-70 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
Steady-state moxifloxacin pharmacokinetics in male Japanese subjects were similar to those determined in Caucasians, with a mean Cmax of 4.1 mcg/mL, an AUC24 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 (CLCR$\geq$ 30 and $\leq$ 60 mL/min) and severe (CLCR<30 mL/min) renal impairment, respectively. The mean systemic exposure (AUC) in these patients was increased by 13%. In the moderate and severe renally 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.

The pharmacokinetics of single dose and multiple dose moxifloxacin were studied in patients with CLCR< 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) to the sulfate conjugate (M1) increased by 1.4-to 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 (AUCss) 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 should be used with caution in these patients.

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 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 3fold in both groups (ranging up to 4.7-and 3.9-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 Tmax following the first intravenous or oral MOXIFLOXACIN 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.

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. The minimum erythematous dose (MED) was measured before and after treatment with Moxifloxacin (200 mg or 400 mg once daily), lomefloxacin (400 mg once daily), or placebo. In this study, the MED measured for both doses of Moxifloxacin were not significantly different from placebo, while lomefloxacin significantly lowered the MED.

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 ultraviolet light (UV) exposure, wearing of sunscreen and protective clothing, the use of other concomitant drugs and the dosage and duration of fluoroquinolone therapy.

Drug-Drug Interactions

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

Antacids and iron significantly reduced bioavailability of moxifloxacin, as observed with other quinolones.

Calcium, digoxin, itraconazole, morphine, probenecid, ranitidine, theophylline, 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 of drugs metabolized by CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 enzymes.

Moxifloxacin had no clinically significant effect on the pharmacokinetics of atenolol, digoxin, glyburide, itraconazole, oral contraceptives, theophylline, and warfarin.

Antacids

When moxifloxacin (single 400 mg tablet dose) was administered two hours before, concomitantly, or 4 hours after an aluminum/magnesium-containing antacid (900 mg aluminum hydroxide and 600 mg magnesium hydroxide as a single oral dose) to 12 healthy volunteers there was a 26%, 60% and 23% reduction in the mean AUC of moxifloxacin, respectively. Moxifloxacin should be taken at least 4 hours before or 8 hours after antacids containing magnesium or aluminum, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc, or didanosine chewable/ buffered tablets or the pediatric powder for oral solution.

Atenolol

In a crossover study involving 24 healthy volunteers (12 male; 12 female), the mean atenolol AUC following a single oral dose of 50 mg atenolol with placebo was similar to that observed when atenolol was given concomitantly with a single 400 mg oral dose of moxifloxacin. The mean C_{max} of single dose atenolol decreased by about 10% following co-administration with a single dose of moxifloxacin.

Calcium

Twelve healthy volunteers were administered concomitant moxifloxacin (single 400 mg dose) and calcium (single dose of 500 mg Ca^{++} dietary supplement) followed by an additional two doses of calcium 12 and 24 hours after moxifloxacin administration. Calcium had no significant effect on the mean AUC of moxifloxacin. The mean Cmax was slightly reduced and the time to maximum plasma concentration was prolonged when moxifloxacin was given with calcium compared to when moxifloxacin was given alone (2.5 hours versus 0.9 hours). These differences are not considered to be clinically significant.

Digoxin

No significant effect of moxifloxacin (400 mg once daily for two days) on digoxin (0.6 mg as a single dose) AUC was detected in a study involving 12 healthy volunteers. The mean digoxin Cmax increased by about 50% during the distribution phase of digoxin. This transient increase in digoxin Cmax is not viewed to be clinically significant. Moxifloxacin pharmacokinetics were similar in the presence or absence of digoxin. No dosage adjustment for moxifloxacin or digoxin is required when these drugs are administered concomitantly.

Glyburide

In diabetics, glyburide (2.5 mg once daily for two weeks pretreatment and for five days concurrently) mean AUC and Cmax were 12% and 21% lower, respectively, when taken with moxifloxacin (400 mg once daily for five days) in comparison to placebo. Nonetheless, blood glucose levels were decreased slightly in patients taking glyburide and moxifloxacin in comparison to those taking glyburide alone, suggesting no interference by moxifloxacin on the activity of glyburide. These interaction results are not viewed as clinically significant.

Iron

When moxifloxacin tablets were administered concomitantly with iron (ferrous sulfate 100 mg once daily for two days), the mean AUC and Cmax of moxifloxacin was reduced by 39% and 59%, respectively. Moxifloxacin should only be taken more than 4 hours before or 8 hours after iron products.

Itraconazole

In a study involving 11 healthy volunteers, there was no significant effect of itraconazole (200 mg once daily for 9 days), a potent inhibitor of cytochrome P4503A4, on the pharmacokinetics of moxifloxacin (a single 400 mg dose given on the 7^{th} day of itraconazole dosing). In addition, moxifloxacin was shown not to affect the pharmacokinetics of itraconazole.

Morphine

No significant effect of morphine sulfate (a single 10 mg intramuscular dose) on the mean AUC and Cmax of moxifloxacin (400 mg single dose) was observed in a study of 20 healthy male and female volunteers.

Oral Contraceptives

A placebo-controlled study in 29 healthy female subjects showed that moxifloxacin 400 mg daily for 7 days did not interfere with the hormonal suppression of oral contraception with 0.15 mg levonorgestrel/0.03 mg ethinylestradiol (as measured by serum progesterone, FSH, estradiol, and LH), or with the pharmacokinetics of the administered contraceptive agents.

Probenecid

Probenecid (500 mg twice daily for two days) did not alter the renal clearance and total amount of moxifloxacin (400 mg single dose) excreted renally in a study of 12 healthy volunteers.

Ranitidine
No significant effect of ranitidine (150 mg twice daily for three days as pretreatment) on the pharmacokinetics of moxifloxacin (400 mg single dose) was detected in a study involving 10 healthy volunteers.

Theophylline
No significant effect of moxifloxacin (200 mg every twelve hours for 3 days) on the pharmacokinetics of theophylline (400 mg every twelve hours for 3 days) was detected in a study involving 12 healthy volunteers. In addition, theophylline was not shown to affect the pharmacokinetics of moxifloxacin. The effect of co-administration of a 400 mg dose of moxifloxacin with theophylline has not been studied, but it is not expected to be clinically significant based on *in vitro* metabolic data showing that moxifloxacin does not inhibit the CYP1A2 isoenzyme.

Warfarin
No significant effect of moxifloxacin (400 mg once daily for eight days) on the pharmacokinetics of R-and S-warfarin (25 mg single dose of warfarin sodium on the fifth day) was detected in a study involving 24 healthy volunteers. No significant change in prothrombin time was observed.

INDICATIONS AND USAGE
Moxif I.V. is indicated for the treatment of adults (≥18years of age) infections causes by susceptible strains of the designated microorganisms in the conditions listed below.

Acute Bacterial Sinusitis caused by *Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhails.*

Acute Bacterial Exacerbation of Chronic Bronchitis caused by *Streptococcus pneumoniae, Haemophilus parainfluenzae, Klebsiella pneumoniae Staphylacoccus aureus, or Moraxella catarrhails.*

Community Acquired Pneumonia (of mild to moderate severity) caused by *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Chlamydia pneumoniae, or Moraxella catarrhails.*

Uncomplicated skin and skin structure infections caused by *Staphyloccus aureus and Streptococcus pyogenes.*

DOSAGE AND ADMINISTRATION
Dosage in Adult Patients
The dose of Moxifloxacin is 400 mg (orally or as an intravenous infusion) once every 24 hours. The duration of therapy depends on the type of infection as described in Table

Table: Dosage and Duration of Therapy in Adult Patients

Type of Infectiona	**Dose Every 24 hours**	**Durationb (days)**
Acute Bacterial Sinusitis	400 mg	10
Acute Bacterial Exacerbation of Chronic Bronchitis (1.2)	400 mg	5
Community Acquired Pneumonia	400 mg	7-14
Uncomplicated Skin and Skin Structure Infections (SSSI) (1.4)	400 mg	7
Complicated SSSI (1.5)	400 mg	7-21
Complicated Intra-Abdominal Infections (1.6)	400 mg	5-14

a) Due to the designated pathogens.
b) Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician

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 IV may be switched to moxifloxacin Tablets when clinically indicated at the discretion of the physician.

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

Moxifloxacin IV should be administered by intravenous infusion only. It is not intended for intra-arterial, intramuscular, intrathecal, intraperitoneal, or subcutaneous administration.

To be used with a pyrogen free I.V. administration set using aseptic technique.

Store in cool dark place. Do not freeze. Protect from light on removal from the manufacturer's original carton.

CONTRAINDICATIONS

- Hypersensitivity to moxifloxacin, other quinolones or to any of the excipients.
- Pregnancy and lactation.
- Patients below 18 years of age.
- Patients with a history of tendon disease/disorder related to quinolone treatment. Both in preclinical investigations and in humans, changes in cardiac electrophysiology have been observed following exposure to moxifloxacin, in the form of QT prolongation. For reasons of drug safety, moxifloxacin is therefore contraindicated in patients with:
- Congenital or documented acquired QT prolongation
- Electrolyte disturbances, particularly in uncorrected hypokalaemia
- Clinically relevant bradycardia
- Clinically relevant heart failure with reduced left-ventricular ejection fraction

- Previous history of symptomatic arrhythmias

Moxifloxacin should not be used concurrently with other drugs that prolong the QT interval. Due to limited clinical data, moxifloxacin is also contraindicated in patients with impaired liver function (Child Pugh C) and in patients with transaminases increase >5 fold ULN.

WARNINGS AND PRECAUTION

Tendinopathy 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 rupture of the Achilles tendon may require surgical repair. Tendinitis and tendon rupture in the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendon sites have also been reported. The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Factors, in addition to age and corticosteroid use, 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. Tendon rupture can occur during or after completion of therapy; cases occurring up to several months after completion of therapy have been reported. moxifloxacin should be discontinued 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.

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 known history of myasthenia gravis.

QT Prolongation

Moxifloxacin 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 (± 26) (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 10 msec (±22) on Day 1 (n=667) and 7 msec (± 24) on Day 3 (n = 667).

The drug should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia and patients receiving Class IA (for example, quinidine, procainamide) or Class III (for example, amiodarone, sotalol) antiarrhythmic 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 with ongoing proarrhythmic conditions, such as clinically significant bradycardia, acute myocardial ischemia. 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. QT prolongation may lead to an increased risk for ventricular arrhythmias including torsade de pointes. 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. Elderly patients using IV 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 quinolone therapy, including moxifloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. moxifloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Oxygen, intravenous steroids, and airway management, including intubation, may be administered as indicated.

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

The drug should be discontinued immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted

Central Nervous System Effects
Fluoroquinolones, including moxifloxacin, may cause central nervous system (CNS) events, including: nervousness, agitation, insomnia, anxiety, nightmares or paranoia.

Convulsions and increased intracranial pressure (including pseudotumor cerebri) have been reported in patients receiving fluoroquinolones. Fluoroquinolones may also cause central nervous system (CNS) events including: 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, the drug should be discontinued and appropriate measures instituted. As with all fluoroquinolones, moxifloxacin should be used with caution 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.

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

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic 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.

Peripheral Neuropathy
Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving fluoroquinolones including moxifloxacin. Symptoms may occur soon after initiation of moxifloxacin and may be irreversible. moxifloxacin should be discontinued 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.

Arthropathic Effects in 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 hypoglycemia and hyperglycemia have been reported with moxifloxacin. In moxifloxacin -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 should be discontinued and appropriate therapy should be initiated immediately.

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 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.

DRUG INTERACTIONS
Antacids, Sucralfate, Multivitamins and other products containing 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, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored if a quinolone is administered concomitantly with warfarin or its derivatives.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)
Although not observed with moxifloxacin in preclinical and clinical trials, the concomitant administration of a nonsteroidal anti-inflammatory drug 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 electrocardiogram. Sotalol, a Class III antiarrhythmic, has been shown to further increase the QTc interval when combined with high doses of intravenous (IV) moxifloxacin in dogs. Therefore, moxifloxacin should be avoided with Class IA and Class III antiarrhythmics.

USE IN SPECIFIC POPULATIONS
Pregnancy
Pregnancy Category C
Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day or 0.24 times the maximum recommended human dose based on systemic exposure (AUC), but decreased fetal body weights and slightly delayed fetal skeletal development (indicative of fetotoxicity) were observed. Intravenous administration of 80 mg/kg/day (approximately 2 times the maximum recommended human dose based on body surface area (mg/m^2) to pregnant rats resulted in maternal toxicity and a marginal effect on fetal and placental weights and the appearance of the placenta. There was no evidence of teratogenicity at intravenous doses as high as 80 mg/kg/day. 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 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. Signs of maternal toxicity in rabbits at this dose included mortality, abortions, marked reduction of food consumption, decreased water intake, body weight loss and hypoactivity. There was no evidence of teratogenicity when pregnant cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (2.5 times the maximum recommended human dose based upon systemic exposure). An increased incidence of smaller fetuses was observed at 100 mg/kg/day. In an oral pre-and postnatal development study observed in rats, effects observed at 500 mg/kg/day included slight increases in duration of pregnancy and prenatal loss, reduced pup birth weight and decreased neonatal survival. Treatment-related maternal mortality occurred during gestation at 500 mg/kg/day in this study.

Nursing Mothers
Moxifloxacin is excreted in the breast milk of rats. Moxifloxacin may also be excreted in human milk. Because of the potential for serious adverse reactions in infants who are nursing from mothers taking 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 to elderly patients especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue moxifloxacin and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur.

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

In trials of intravenous use, 42% of moxifloxacin patients were greater than or equal to 65 years of age, and 23% were greater than or equal to 75 years of age. The clinical trial data demonstrate that the safety of intravenous moxifloxacin 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 pointes (for example, known QT prolongation, uncorrected hypokalemia).

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).

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.

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 quinolones, 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 CHOIHGPRT

mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 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 (mg/m^2). At 500 mg/kg there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

ADVERSE REACTIONS

Serious and Otherwise Important Adverse Reactions

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

- Tendinopathy and Tendon Rupture
- QT Prolongation
- Hypersensitivity Reactions
- Other Serious and Sometimes Fatal Reactions
- Central Nervous System Effects
- Clostridium difficile-Associated Diarrhea
- Peripheral Neuropathy that may be irreversible
- Photosensitivity/Phototoxicity
- Development of Drug Resistant Bacteria

Clinical Trial Experience

The data described below reflect exposure to moxifloxacin in 14981 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 PO, IV, or sequentially (IV followed by PO). 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 5.0% of patients overall, 4.1% of patients treated with 400 mg PO, 3.9% with 400 mg IV and 8.2% with sequential therapy 400 mg PO/IV. The most common adverse events leading to discontinuation with the 400 mg PO doses were nausea (0.8%), diarrhea (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/PO sequential dose were diarrhea (0.5%), 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 **Tables 1** and **Table 2**, respectively. The most common adverse drug reactions (≥3%) are nausea, diarrhea, headache, and dizziness.

Table 1 Common (≥ 1.0%) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin

System Organ Class	Adverse Reactionsa	% (N=14,981)
Blood and Lymphatic System Disorders	Anemia	1.1
Gastrointestinal Disorders	Nausea	6.9
	Diarrhea	6.0
	Vomiting	2.4
	Constipation	1.9
	Abdominal pain	1.5
	Abdominal pain upper	1.1
	Dyspepsia	1.0
General Disorders and Administration Site Conditions	Pyrexia	1.1
Investigations	Alanine aminotransferase increased	1.1
Metabolism and Nutritional Disorder	Hypokalemia	1
Nervous System Disorders	Headache	4.2
	Dizziness	3.0
Psychiatric Disorders	Insomnia	1.9

Table 2 Less Common (0.1 to <1.0%) Adverse Reactions Reported in Active-Controlled Clinical Trials with Moxifloxacin (N=14,981)

System Organ Class	Adverse Reactionsa
Blood and Lymphatic System Disorders	Thrombocythemia
	Eosinophilia
	Neutropenia
	Thrombocytopenia
	Leukopenia
	Leukocytosis
Cardiac Disorders	Atrial fibrillation
	Palpitations
	Tachycardia
	Cardiac failure congestive
	Angina pectoris
	Cardiac failure
	Cardiac arrest
	Bradycardia
Ear and Labyrinth Disorders	Vertigo
	Tinnitus
Gastrointestinal Disorders	Dry mouth
	Abdominal discomfort
	Flatulence
	Abdominal distention
	Gastritis

	Gastroesophageal reflux disease
General Disorders and Administration Site Conditions	Fatigue Chest pain Asthenia Edema peripheral Pain Malaise Infusion site extravasation Edema 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
Investigations	Aspartate aminotransferase increased Gamma-glutamyltransferase increased Blood alkaline phosphatase increased Hepatic enzyme increased Electrocardiogram QT prolonged Blood lactate dehydrogenase increased Platelet count increased Blood amylase increased Blood glucose increased Lipase increased Hemoglobin decreased Blood creatinine increased Transaminases increased White blood cell count increased Blood urea increased Liver function test abnormal Hematocrit decreased Prothrombin time prolonged Eosinophil count increased Activated partial thromboplastin time prolonged Blood bilirubin increased Blood triglycerides increased Blood uric acid increased Blood pressure increased
Metabolism and Nutrition Disorders	Hyperglycemia Anorexia Hypoglycemia

	Hyperlipidemia Decreased appetite Dehydration
Musculoskeletal and Connective Tissue Disorders	Back pain Pain in extremity Arthralgia Myalgia Muscle spasms Musculoskeletal chest pain Musculoskeletal pain
Nervous System Disorders	Dysgeusia Somnolence Tremor Lethargy Paresthesia Tension headache Hypoesthesia Syncope
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	Dyspnea Asthma Wheezing Bronchospasm
Skin and Subcutaneous Tissue Disorders	Rash Pruritus Hyperhidrosis Erythema Urticaria Dermatitis allergic Night sweats
Vascular disorders	Hypertension Hypotension Phlebitis

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 MCH, neutrophils, WBCs, PT ratio, ionized calcium, chloride, albumin, globulin, bilirubin; decreases in hemoglobin, RBCs, neutrophils, eosinophils, basophils, PT ratio, glucose, 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.

Postmarketing Experience
Table 3 lists adverse reactions that have been identified during post-approval use of Moxifloxacin. Because these events 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 3: Postmarketing Reports of Adverse Drug Reactions

System/Organ Class	Adverse Reaction
Blood and Lymphatic System Disorders	Agranulocytosis Pancytopenia
Cardiac Disorders	Ventricular tachyarrhythmias (including in very rare cases cardiac arrest and torsade de pointes, and usually in patients with concurrent severe underlying proarrhythmic conditions)
Ear and Labyrinth Disorders	Hearing impairment, including deafness (reversible in majority of cases)
Eye Disorders	Vision loss (especially in the course of CNS reactions, transient in majority of cases)
Hepatobiliary Disorders	Hepatitis (predominantly cholestatic) Hepatic failure (including fatal cases) Jaundice Acute hepatic necrosis
Immune System Disorders	Anaphylactic reaction Anaphylactic shock Angioedema (including laryngeal edema)
Musculoskeletal and Connective Tissue Disorders	Tendon rupture
Nervous System Disorders	Altered coordination Abnormal gait Myasthenia gravis (exacerbation of) Muscle weakness Peripheral neuropathy (that may be irreversible), polyneuropathy
Psychiatric Disorders	Psychotic reaction (very rarely culminating in self-injurious behavior, such as suicidal ideation/thoughts or suicide attempts
Renal and Urinary Disorders	Renal dysfunction Interstitial nephritis

Respiratory, Thoracic and Mediastinal Disorders	Allergic pneumonitis
Skin and Subcutaneous Tissue Disorders	Photosensitivity/phototoxicity reaction Stevens-Johnson syndrome Toxic epidermal necrolysis

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 more prominent and more consistent across the systemic fluoroquinolone drug class. The mental health side effects to be added to or updated across all the fluoroquinolones are:

- disturbances in attention
- disorientation
- agitation
- nervousness
- memory impairment
- Serious disturbances in mental abilities called delirium.

OVERDOSE
No specific countermeasures after accidental overdose are recommended. General symptomatic therapy should be initiated. Concomitant administration of charcoal with a dose of 400 mg oral moxifloxacin will reduce systemic availability of the drug by more than 80%. The use of charcoal early during absorption may be useful to prevent excessive increase in the systemic exposure to moxifloxacin in cases of oral overdose.

PRESENTATION:
Each 100ml infusion contains Moxifloxacin Hydrochloride B.P. equivalent to moxifloxacin 400 mg as a single dose container. Moxif IV is available as 100ml FFS plastic Bottle.

STORAGE AND HANDLING INSTRUCTIONS:
Store in cool and dark place. Do not freeze. Protect from light on removal from manufacturer's original carton. To be used with a pyrogen free I.V. administration set using aseptic technique.
STERILE, NON-PYROGENIC, ISOTONIC, SINGLE DOSE CONTAINER FOR INTRAVENOUS USE ONLY.

CAUTION:
Do not use infusion if the contents are not clear or show any particulate matter or if the bottle is leaking.

WARNING:
Do not add product of high pH. Recommended pH=4-5.5.

EXPIRY DATE:
Do not use later than date of expiry.

MARKETED BY

TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

IN/ MOXIF I.V. 400 mg/JAN-19/03/PI