Zilfom®

زِلفوم

(Moxifloxacin Tablet USP)

COMPOSITION
Each film coated tablet contains:
Moxifloxacin HCl USP equivalent to
Moxifloxacin..... 400mg
(USP Specs.)

BLACK BOX WARNING
WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAL NERVOUS SYTEM EFFECTS and EXACERBATION OF MYASTHENIA GRAVIS
• Fluoroquinolones, including Moxifloxacin, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together [see Warnings and Precautions], including:
o Tendinitis and tendon rupture
o Peripheral neuropathy
o Central nervous system effects

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

• Fluoroquinolones, including Moxifloxacin, may exacerbate muscle weakness in patients with myasthenia gravis. Avoid Moxifloxacin in patients with known history of myasthenia gravis.

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

DESCRIPTION
Zilfom (moxifloxacin hydrochloride) is a synthetic antibacterial agent for oral administration. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt of 1-cyclopropyl-7-[(S,S)-2,8diazabicyclo[4.3.0]non-8-yl]-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3 quinoline carboxylic acid. Its empirical formula is $C_{21}H_{24}FN_3O_4$*HCl

CLINICAL PHARMACOLOGY
Pharmacodynamics
Pharmacotherapeutic group: Quinolone antibacterials, fluoroquinolones.

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.

Antimicrobial Activity
Gram-positive bacteria
Enterococcus faecalis, Staphylococcus aureus, Streptococcus anginosus, Streptococcus constellatus, Streptococcus pneumoniae (including multi-drug resistant isolates [MDRSP] **) Streptococcus pyogenes.

**MDRSP, Multi-drug resistant Streptococcus pneumoniae includes isolates previously known as PRSP (Penicillin resistant S. pneumoniae), and are isolates resistant to two or more of the following antibiotics: penicillin (MIC) ≥2 mcg/mL), 2nd generation cephalosporins (for example, cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

Gram-negative bacteria
Enterobacter cloacae, Escherichia coli, Haemophilus influenza, Haemophilus parainfluenzae, Klebsiella pneumonia, Moraxella catarrhalis, Proteus mirabilis, Yersinia pestis.

Anaerobic bacteria
Bacteroides fragilis, Bacteroides thetaiotaomicron, Clostridium perfringens, Peptostreptococcus species.

Other microorganisms
Chlamydophila pneumonia, Mycoplasma pneumonia

The following in vitro data are available, but their clinical significance is unknown.

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

Mechanism of Resistance
The mechanism of action for fluoroquinolones, including moxifloxacin, is different from that of macrolides, beta-lactams, aminoglycosides, or tetracyclines; therefore, microorganisms resistant to these classes of drugs may be susceptible to moxifloxacin. Resistance to fluoroquinolones occurs primarily by a mutation in topoisomerase II (DNA gyrase) or topoisomerase IV genes, decreased outer membrane permeability or drug efflux .

Pharmacokinetics
• Absorption
Following oral administration moxifloxacin is rapidly and almost completely absorbed. The absolute bioavailability amounts to approximately 91%.

Pharmacokinetics are linear in the range of 50 - 800 mg single dose and up to 600 mg once daily dosing over 10 days. Following a 400 mg oral dose peak concentrations of 3.1 mg/l are reached within 0.5 - 4 h post administration. Peak and trough plasma concentrations at steady-state (400 mg once daily) were 3.2 and 0.6 mg/l, respectively. At steady-state the exposure within the dosing interval is approximately 30% higher than after the first dose.

• Distribution
Moxifloxacin is distributed to extravascular spaces rapidly; after a dose of 400 mg an AUC of 35 mˑghˑl is observed. The steady-state volume of distribution (Vss) is approximately 2 l/kg. In vitro and ex vivo experiments showed a protein binding of approximately 40 - 42% independent of the concentration of the drug. Moxifloxacin is mainly bound to serum albumin.

• 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.

• Elimination
Moxifloxacin is eliminated from plasma with a mean terminal half life of approximately 12 hours. The mean apparent total body clearance following a 400 mg dose ranges from 179 to 246 ml/min. Renal clearance amounted to about 24-53 ml/min suggesting partial tubular reabsorption of the drug from the kidneys.

After a 400 mg dose, recovery from urine (approximately 19% for unchanged drug, approximately 2.5% for M1, and approximately 14% for M2) and faeces (approximately 25% of unchanged drug, approximately 36% for M1, and no recovery for M2) totalled to approximately 96%.
Concomitant administration of moxifloxacin with ranitidine or probenecid did not alter renal clearance of the parent drug.

Pharmacokinetics in special populations
Elderly and patients with low body weight
Higher plasma concentrations are observed in healthy volunteers with low body weight (such as women) and in elderly volunteers.

Renal impairment
The pharmacokinetic properties of moxifloxacin are not significantly different in patients with renal impairment (including creatinine clearance > 20 ml/min/1.73 m2). As renal function decreases, concentrations of the M2 metabolite (glucuronide) increase by up to a factor of 2.5 (with a creatinine clearance of < 30 ml/min/1.73 m2).

Hepatic impairment
On the basis of the pharmacokinetic studies carried out so far in patients with liver failure (Child Pugh A, B), it is not possible to determine whether there are any differences compared with healthy volunteers. Impaired liver function was associated with higher exposure to M1 in plasma, whereas exposure to parent drug was comparable to exposure in healthy volunteers. There is insufficient experience in the clinical use of moxifloxacin in patients with impaired liver function.

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

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

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

2. Complicated Skin and Skin Structure Infections
Zilfom is indicated in adult patients for the treatment of Complicated Skin and Skin Structure Infections caused by susceptible isolates of methicillin-susceptible Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, or Enterobacter cloacae.

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

4. Plague
Zilfom is indicated in adult patients for the treatment of plague, including pneumonic and septicemic plague, due to susceptible isolates of Yersinia pestis and prophylaxis of plague in adult patients. Efficacy studies of moxifloxacin could not be conducted in humans with plague for feasibility reasons. Therefore this indication is based on an efficacy study conducted in animals only.

5. Acute Bacterial Sinusitis
Zilfom is indicated in adult patients (18 years of age and older) for the treatment of acute bacterial sinusitis (ABS) caused by susceptible isolates of Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis.

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

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

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

DOSAGE AND ADMINISTRATION
• Adult dosage
The dose of Zilfom is 400 mg tablet taken orally once every 24 hours. The duration of therapy depends on the type of infection as described below.

Indication	Duration (days)
Community Acquired Pneumonia	7–14
Uncomplicated Skin and Skin Structure Infections (SSSI)	7
Complicated SSSI	7–21
Complicated Intra-Abdominal Infections	5–14
Plague	10–14
Acute Bacterial Sinusitis (ABS)	10
Acute Bacterial Exacerbation of Chronic Bronchitis (ABECB)	5

• Dosage adjustment
Renal/hepatic impairment
No adjustment of dosage is required in patients with mild to severely impaired renal function or in patients on chronic dialysis i.e. haemodialysis and continuous ambulatory peritoneal dialysis.

There is insufficient data in patients with impaired liver function. Due to limited clinical data, moxifloxacin is contraindicated in patients with impaired liver function (Child Pugh C).

Elderly
No adjustment of dosage is required in the elderly and in patients with low bodyweight.

Paediatric population
Moxifloxacin is contraindicated in children and adolescents (< 18 years). Efficacy and safety of moxifloxacin in children and adolescents have not been established.

CONTRAINDICATIONS
Zilfom is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antibacterials

WARNING AND PRECAUTIONS
Disabling and Potentially Irreversible Serious Adverse Reactions Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and Central Nervous System Effects
Fluoroquinolones, including Moxifloxacin, have been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions can occur within hours to weeks after starting Moxifloxacin. Patients of any age or without pre-existing risk factors have experienced these adverse reactions.

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

Tendinitis and Tendon Rupture
Fluoroquinolones, including Moxifloxacin, have been 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 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 immediately if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendinitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug. Avoid fluoroquinolones, including Moxifloxacin, in patients who have a history of tendon disorders or who have experienced tendinitis or tendon rupture.

Fluoroquinolones, including Moxifloxacin, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving fluoroquinolones including 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.

Central Nervous System Effects
Fluoroquinolones, including Moxifloxacin, have been associated with an increased risk of central nervous system (CNS) reactions, including: convulsions and increased intracranial pressure (including pseudotumor cerebri) and toxic psychosis, Fluoroquinolones may also cause CNS reactions of nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression, and, suicidal thoughts or acts. These adverse reactions may occur following the first dose. If these reactions occur in patients receiving Moxifloxacin, discontinue Moxifloxacin immediately and institute appropriate measures. As with all fluoroquinolones, use Moxifloxacin when the benefits of treatment exceed the risks in patients with known or suspected CNS disorders (for example, severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold.

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

QT Prolongation
Moxifloxacin has been shown to prolong the QTc interval on the electrocardiogram in some patients. In the analysis of ECGs obtained in the clinical trial program, QTc prolongation with Moxifloxacin was 6 msec ± 26 msec, 1.4% compared to baseline. As women tend to have a longer baseline QTc interval compared with men, they may be more sensitive to QTc-prolonging medications. Elderly patients may

also be more susceptible to drug-associated effects on the QT interval.

Medication that can reduce potassium levels should be used with caution in patients receiving Moxifloxacin.

Moxifloxacin should be used with caution in patients with ongoing proarrhythmic conditions (especially women and elderly patients), such as acute myocardial ischaemia or QT prolongation as this may lead to an increased risk for ventricular arrhythmias (incl. torsade de pointes) and cardiac arrest. The magnitude of QT prolongation may increase with increasing concentrations of the drug. Therefore, the recommended dose should not be exceeded.

If signs of cardiac arrhythmia occur during treatment with Moxifloxacin, treatment should be stopped and an ECG should be performed.

Hypersensitivity/allergic reactions
Hypersensitivity and allergic reactions have been reported for fluoroquinolones including Moxifloxacin after first administration. Anaphylactic reactions can progress to a life-threatening shock, even after the first administration. In cases of clinical manifestations of severe hypersensitivity reactions Moxifloxacin should be discontinued and suitable treatment (e.g. treatment for shock) initiated.

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.

Patients predisposed to seizures
Quinolones are known to trigger seizures. Use should be with caution in patients with CNS disorders or in the presence of other risk factors which may predispose to seizures or lower the seizure threshold. In case of seizures, treatment with Moxifloxacin should be discontinued and appropriate measures instituted.

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypoaesthesia, dysaesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with Moxifloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition.

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.

ADVERSE REACTIONS

System Organ Class (MedDRA)	Common	Uncommon	Rare	Very Rare	Not known
Infections and infestations	Superinfections due to resistant bacteria or fungi e.g. oral and vaginal candidiasis				
Blood and lymphatic system disorders		Anaemia Leucopenia(s) Neutropenia Thrombocytopenia Thrombocythemia Blood eosinophilia Prothrombin time prolonged/INR increased		Prothrombin level increased/INR decreased Agranulocytosis Pancytopenia	
Immune system disorders		Allergic reaction	Anaphylaxis incl. very rarely life-threatening shock Allergic oedema / angiooedema (incl. laryngeal oedema, potentially life-threatening)		
Endocrine disorders				Syndrome of inappropriate antidiuretic hormone secretion (SIADH)	
Metabolism and nutrition disorders		Hyperlipidemia	Hyperglycemia Hyperuricemia	Hypoglycemia Hypoglycaemic coma	
Psychiatric disorders		Anxiety reactions Psychomotor hyperactivity/ agitation	Emotional lability Depression (in very rare cases potentially culminating in self-injurious behaviour, such as suicidal ideations/ thoughts, or suicide attempts) Hallucination Delirium	Depersonalization Psychotic reactions (potentially culminating in self- injurious behaviour, such as suicidal ideations/ thoughts, or suicide attempts)	
Nervous system disorders	Headache Dizziness	Par- and Dysaesthesia Taste disorders (incl. ageusia in very rare cases) Confusion and disorientation Sleep disorders (predominantly insomnia) Tremor Vertigo Somnolence	Hypoaesthesia Smell disorders (incl. anosmia) Abnormal dreams Disturbed coordination (incl. gait disturbances, esp. due to dizziness or vertigo) Seizures incl. grand mal convulsions Disturbed attention Speech disorders Amnesia Peripheral neuropathy and polyneuropathy	Hyperaesthesia	
Eye disorders		Visual disturbances incl. diplopia and blurred vision (especially in the course of CNS reactions)	Photophobia	Transient loss of vision (especially in the course of CNS reactions) Uveitis and bilateral acute iris transillumination	
Ear and labyrinth disorders			Tinnitus Hearing impairment incl. deafness (usually reversible)		
Cardiac disorders	QT prolongation in patients with hypokalaemia	QT prolongation Palpitations Tachycardia Atrial fibrillation Angina pectoris	Ventricular tachyarrhythmias Syncope (i.e., acute and short lasting loss of consciousness)	Unspecified arrhythmias Torsade de Pointes Cardiac arrest	
Vascular disorders		Vasodilatation	Hypertension Hypotension	Vasculitis	
Respiratory, thoracic and mediastinal disorders		Dyspnea (including asthmatic conditions)			
Gastrointestinal disorders	Nausea Vomiting Gastrointestinal and abdominal pains Diarrhoea	Decreased appetite and food intake Constipation Dyspepsia Flatulence Gastritis Increased amylase	Dysphagia Stomatitis Antibiotic associated colitis (incl. pseudo-membranous colitis, in very rare cases associated with life-threatening complications)		
Hepatobiliary disorders	Increase in transaminases	Hepatic impairment (incl. LDH increase) Increased bilirubin Increased gamma-glutamyl-transferase Increase in blood alkaline phosphatase	Jaundice Hepatitis (predominantly cholestatic)	Fulminant hepatitis potentially leading to life-threatening liver failure	
Skin and subcutaneous tissue disorders		Pruritus Rash Urticaria Dry skin		Bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis (potentially life-threatening)	Acute Generalised Exanthematous Pustulosis (AGEP)
Musculoskeletal and connective tissue disorders		Arthralgia Myalgia	Tendonitis Muscle cramp Muscle twitching Muscle weakness	Tendon rupture Arthritis Muscle rigidity Exacerbation of symptoms of myasthenia gravis	Rhabdomyolysis
Renal and urinary disorders		Dehydration	Renal impairment (incl. increase in BUN and creatinine) Renal failure		
General disorders and administration site conditions		Feeling unwell (predominantly asthenia or fatigue) Painful conditions (incl. pain in back, chest, pelvic and extremities) Sweating	Odema		

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

Warfarin
Fluoroquinolones, including Moxifloxacin, have been reported to enhance the anticoagulant effects of warfarin or its derivatives in the patient population. In addition, infectious disease and its accompanying inflammatory process, age, and general status of the patient are risk factors for increased anticoagulant activity. Therefore the prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored if Moxifloxacin is administered concomitantly with warfarin or its derivatives.

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

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

Drugs that Prolong QT
There is limited information available on the potential for a pharmacodynamic interaction in humans between Moxifloxacin and other drugs that prolong the QTc interval of the electrocardiogram. Sotalol, a Class III antiarrhythmic, has been shown to further increase the QTc interval when combined with high doses of intravenous Moxifloxacin in dogs. Therefore, Moxifloxacin should be avoided with Class IA and Class III antiarrhythmics.

USE IN SPECIAL POPULATIONS

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

• Nursing mother
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.

• Pediatrics
Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established.

• Elderly
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.

• 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.

OVER DOSAGE
No specific countermeasures after accidental overdose are recommended. In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. 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
Zilfom 400mg: Pack of 5 Tablets

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
Call pharmassist helpline 0800-82222
Monday to friday 9:00 am to 6:00 pm
Or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔
دوا کے ممکنہ منفی اثرات کے متعلق reports@pharmevo.biz پر مطلع کریں۔

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