MOXISPEY

Instructions for the medicinal product

Trade name: Moxispey.
International Nonproprietary Name: Moxifloxacin.
Dosage form: Solution for injection.
Composition: Each 100 ml contains:
Moxifloxacin HCl BP eq. to Moxifloxacin 400 mg;
Excipients q.s.
Pharmacotherapeutic group: Quinolone antibacterials, fluoroquinolones.
ATC Code: J01MA14.
Pharmacological properties
Pharmacodynamics:
Moxifloxacin is active against a broad spectrum of gram-positive and gram-negative microorganisms, anaerobic, acid-resistant and atypical bacteria: Mycoplasmas pp., Chlamydias pp., Legionellas pp. Effective against bacterial strains that are resistant to beta-lactam antibiotics and macrolides.
It is active against most strains of microorganisms: Gram - Staphylococcusaureus (including strains that are insensitive to methicillin), Streptococcus pneumoniae (including strains resistant to penicillin and macrolides), Streptococcuspyogenes (group A), Gram – Haemophilus influenzae (including both producing and non-producing beta-lactamase strains), Haemophilus para influenzae, Klebsiella pneumoniae, Moraxellacatarrhalis (including both producing and non-producing beta-lactamase strains), Escherichiacoli, Enterobactercloacae; atypical – Chlamydia pneumoniae, Mycoplasma pneumoniae.
The following micro-organisms susceptible to moxifloxacin, however the safety and efficacy in the treatment of his infection has not been established. *Gram-positive microorganisms:* Streptococcusmilleri, Streptococcusmitis, Streptococcusa galactiae, Streptococcus dysgalactiae, Staphylococcuscohnii, Staphylococcusepidermidis (including strains that are sensitive to methicillin), Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcuss aprophyticus, Staphylococcuss imulans, Corynebacterium diphtheriae.
Gram-negative microorganisms: Bordetella pertussis, Klebsiella oxytoca, Enterobacter aerogenes, Enterobacter agglomerans, Enterobacter intermedius, Enterobacter sakazakii, Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia rettgeri, Providencia stuartii.
Anaerobic Microorganisms: Bacteroides distasonis, Bacteroides eggerthii, Bacteroides fragilis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides uniforms, Fusobacterium spp., Porphyromonas spp., Porphyromonas anaerobius, Porphyromonas asaccharolyticus, Porphyromonas magnus, Prevotella spp., Propionibacterium spp., Streptococcus pyogenes, Streptococcus branched.
Atypical organisms: Legionella pneumophila, Coxiell aburnetii.
Moxifloxacin inhibits bacterial type II topoisomerases (DNA gyrase and topoisomerase IV) that are required for bacterial DNA replication, transcription and repair.
Resistance to fluoroquinolones can arise through mutations in DNA gyrase and topoisomerase IV. Other mechanisms may include over-expression of efflux pumps, impermeability, and protein-mediated protection of DNA gyrase. Cross resistance should be expected between moxifloxacin and other fluoroquinolones.
The activity of moxifloxacin is not affected by mechanisms of resistance that are specific to antibacterial agents of other classes.
Pharmacokinetics:
After a single 400 mg intravenous 1 hour infusion peak plasma concentrations of approximately 4.1 mg/l were observed at the end of the infusion corresponding to a mean increase of approximately 26% relative to those seen after oral administration (3.1 mg/l). The AUC value of approximately 39 mg·h/l after i.v. administration is only slightly higher than that observed after oral administration (35 mg·h/l) in accordance with the absolute bioavailability of approximately 91%.
In patients, there is no need for age or gender related dose adjustment on intravenous moxifloxacin.
Moxifloxacin is distributed to extravascular spaces rapidly. The steady-state volume of distribution (Vss) is approximately 2 l/kg. Moxifloxacin is mainly bound to serum albumin. Maximum concentrations of 5.4 mg/kg and 20.7 mg/l (geometric mean) were reached in bronchial mucosa and epithelial lining fluid, respectively, 2.2 h after an oral dose. The corresponding peak concentration in alveolar macrophages amounted to 56.7 mg/kg. In skin blister fluid concentrations of 1.75 mg/l were observed 10 h after intravenous administration. In the interstitial fluid unbound concentration time profiles similar to those in plasma were found with unbound peak concentrations of 1.0 mg/l (geometric mean) reached approximately 1.8 h after an intravenous dose.
Moxifloxacin undergoes Phase II biotransformation and is excreted via renal (approximately 40%) and biliary/faecal (approximately 60%) pathways as unchanged drug as well as in the form of a sulpho-compound (M1) and a glucuronide (M2). M1 and M2 are the only metabolites relevant in humans, both are microbiologically inactive.
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. Following a 400 mg intravenous infusion recovery of unchanged drug from urine was approximately 22% and from faeces approximately 26%. Recovery of the dose (unchanged drug and metabolites) totalled to approximately 98% after intravenous administration of the drug. Renal clearance amounted to about 24 - 53 ml/min suggesting partial tubular reabsorption of the drug from the kidneys. Concomitant administration of moxifloxacin with ranitidine or probenecid did not alter renal clearance of the parent drug.
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:
There is insufficient experience in the clinical use of moxifloxacin in patients with impaired liver function.
Indications for use:
- Acute sinusitis;
- Exacerbation of chronic bronchitis;
- Community-acquired pneumonia;
- Uncomplicated and complicated skin and soft tissues (including infected diabetic foot);
- Complicated intra-abdominal infection including polymicrobial infections (such as abstsedirovanie);
- Uncomplicated inflammatory diseases of the pelvic organs (including salpingitis and endometritis).

Contraindications:
- Hypersensitivity to moxifloxacin, other quinolones;
- Patients below 18 years of age;
- Pregnancy and lactation;
- Patients with a history of tendon disease/disorder related to quinolone treatment.

Precautions: Should be used 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, patients with any condition pre-disposing to cardiac arrhythmias (e.g. acute myocardial ischaemia) because they may have an increased risk of developing ventricular arrhythmias (incl. torsade de pointes) and cardiac arrest, hypokalemia, bradycardia, acute myocardial ischemia, concomitantly with drugs that prolong QT interval, severe liver failure.
Pregnancy and lactation:
The safety of moxifloxacin in human pregnancy has not been evaluated. Moxispey must not be used in pregnant women.
There is no data available in lactating or nursing women. Breast-feeding is contraindicated during Moxispey therapy.
Dosage and directions for use:
For intravenous use. Constant infusion over 60 minutes.
If medically indicated the solution for infusion can be administered via a T-tube, together with compatible infusion solutions.
The recommended dose is 400 mg Moxispey, infused once daily.
Initial intravenous treatment may be followed by oral treatment with moxifloxacin 400 mg tablets, when clinically indicated.
In clinical studies most patients switched to oral therapy within 4 days for Community acquired pneumonia (CAP) or 6 days for Complicated skin and skin structure infections(cSSSI). The recommended total duration of intravenous and oral treatment is 7 - 14 days for CAP and 7 - 21 days for cSSSI.
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.
Other special populations:
No adjustment of dosage is required in the elderly and in patients with low bodyweight.
Side-effects:
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), very rare (< 1/10,000).
Respiratory, thoracic and mediastinal disorders: uncommon - Dyspnea (including asthmatic conditions).
Gastrointestinal disorders: common - nausea, vomiting, abdominal pain, diarrhea. Uncommon - decreased appetite and food intake, constipation, dyspepsia, flatulence, gastritis, Increased amylase. Rare - Dysphagia, stomatitis, antibiotic-associated colitis (incl. pseudo-membranous colitis, in very rare cases associated with life-threatening).
Nervous system: Common - dizziness, headache. Uncommon - Par- and Dysaesthesia, taste disorders (incl. ageusia in very rare cases), confusion and disorientation, Sleep disorders (predominantly insomnia), tremor, vertigo, somnolence. Rare - 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. Very Rare - hyperaesthesia.
Psychiatric disorders: Uncommon - Anxiety reactions, psychomotor hyperactivity/ agitation. Rare - emotional lability, depression (in very rare cases potentially culminating in self-injurious behaviour, such as suicidal ideations/ thoughts, or suicide attempts), hallucination. Very rare - depersonalization, psychotic reactions (potentially culminating in self-injurious behaviour, such as suicidal ideations/ thoughts, or suicide attempts).
Cardiac disorders: Common: - QT prolongation in patients with hypokalaemia. Uncommon - QT prolongation, palpitations, tachycardia, atrial fibrillation, angina pectoris. Rare - ventricular tachyarrhythmias, syncope (i.e., acute and short lasting loss of consciousness). Very rare - unspecified arrhythmias, torsade de Pointes, cardiac arrest.
Blood and lymphatic system disorders: Uncommon - Anaemia, Leucopenia(s), Neutropenia, Thrombocytopenia, Thrombocythemia, Blood eosinophilia, Prothrombin time prolonged/ INR increased. Very rare - Prothrombin level increased/ INR decreased, Agranulocytosis.
Musculoskeletal andconnective tissue disorders: Uncommon - arthralgia, myalgia. Rare - tendonitis, muscle cramp, muscle twitching, muscle weakness. Very rare - Tendon rupture, Arthritis, Muscle rigidity, Exacerbation of symptoms of myasthenia gravis.
Renal and urinary disorders: Uncommon - dehydration. Rare - renal impairment (incl. increase in BUN and creatinine), renal failure.
Skin and subcutaneous tissue disorders: Uncommon - pruritus, rash, urticaria, dry skin. Very rare - Bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis.
Eye disorders: Uncommon - visual disturbances incl. diplopia and blurred vision (especially in the course of CNS reactions). Very rare - transient loss of vision (especially in the course of CNS reactions.
Ear and labyrinth disorders: Rare - tinnitus, hearing impairment incl. deafness (usually reversible).
General disorders and administration site conditions: Common - Injection and infusion site reactions. Feeling unwell (predominantly asthenia or fatigue), painful conditions (incl. pain in back, chest, pelvic and extremities), swelling, infusion site (thrombo-) phlebitis.
Metabolism and nutrition disorders: Uncommon - hyperlipidemia. Rare - hyperglycemia, hyperuricemia.
Overdose:
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 or intravenous moxifloxacin will reduce systemic availability of the drug by more than 80% or 20% respectively. 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.
Drug interaction:
An additive effect on QT interval prolongation of moxifloxacin and other medicinal products that may prolong the QTc interval cannot be excluded. This might lead to an increased risk of ventricular arrhythmias, including torsade de pointes. Therefore, co-administration of moxifloxacin with any of the following medicinal products is contraindicated: anti-arrhythmics class IA (e.g. quinidine, hydroquinidine, disopyramide); anti-arrhythmics class III (e.g. amiodarone, sotalol, dofetilide, ibutilide); antipsychotics (e.g. phenothiazines, pimozide, sertindole, haloperidol, sultopride); tricyclic antidepressive agents; certain antimicrobial agents (saquinavir, sparfloxacin, erythromycin IV, pentamidine, antimalarials particularly halofantrine); certain antihistaminics (terfenadine, astemizole, mizolastine); others (cisapride, vincamine IV, bepridil, diphemanil).
Moxifloxacin should be used with caution in patients who are taking medication that can reduce potassium levels (e.g. loop and thiazide-type diuretics, laxatives and enemas [high doses], corticosteroids, amphotericin B) or medication that is associated with clinically significant bradycardia.
No precaution is required for use with digoxin.
The combination of glibenclamide and moxifloxacin could theoretically result in a mild and transient hyperglycaemia. However, the observed pharmacokinetic changes for glibenclamide did not result in changes of the pharmacodynamic parameters (blood glucose, insulin). Therefore no clinically relevant interaction was observed between moxifloxacin and glibenclamide.
A large number of cases showing an increase in oral anticoagulant activity have been reported in patients receiving antibacterial agents, especially fluoroquinolones, macrolides, tetracyclines, cotrimoxazole and some cephalosporins. The infectious and inflammatory conditions, age and general status of the patient appear to be risk factors. Under these circumstances, it is difficult to evaluate whether the infection or the treatment caused the INR (international normalised ratio) disorder. A precautionary measure would be to more frequently monitor the INR. If necessary, the oral anticoagulant dosage should be adjusted as appropriate.
Clinical studies have shown no interactions following concomitant administration of moxifloxacin with: ranitidine, probenecid, oral contraceptives, calcium supplements, morphine administered parenterally, theophylline, cyclosporine or itraconazole.
Considering these results a metabolic interaction via cytochrome P450 enzymes is unlikely.
Moxifloxacin has no clinically relevant interaction with food including dairy products.
The following solutions are incompatible with Moxispey solution for infusion: Sodium chloride 10% and 20% solutions, Sodium bicarbonate 4.2% and 8.4% solutions.
Cautions:
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 these cases Moxispey should be discontinued and suitable treatment (e.g. treatment for shock) initiated.
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.
Cases of bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with moxifloxacin. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.
In case of seizures, treatment with Moxispey should be discontinued and appropriate measures instituted.
Patients under treatment with Moxispey should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop.
Psychiatric reactions may occur even after the first administration of quinolones, including moxifloxacin. In very rare cases depression or psychotic reactions have progressed to suicidal thoughts and self-injurious behaviour such as suicide attempts. In the event that the patient develops these reactions, Moxispey should be discontinued and appropriate measures instituted. Caution is recommended if moxifloxacin is to be used in psychotic patients or in patients with history of psychiatric disease.
Antibiotic-associated diarrhoea (AAD) and antibiotic-associated colitis (AAC), including pseudomembranous colitis and Clostridium difficile-associated diarrhoea, has been reported in association with the use of broad spectrum antibiotics including moxifloxacin and may range in severity from mild diarrhoea to fatal colitis. Therefore it is important to consider this diagnosis in patients who develop serious diarrhoea during or after the use of moxifloxacin. If AAD or AAC is suspected or confirmed, ongoing treatment with antibacterial agents, including moxifloxacin, should be discontinued and adequate therapeutic measures should be initiated immediately. Furthermore, appropriate infection control measures should be undertaken to reduce the risk of transmission. Drugs inhibiting peristalsis are contraindicated in patients who develop serious diarrhoea.
Moxifloxacin should be used with caution in patients with myasthenia gravis because the symptoms can be exacerbated.
Tendon inflammation and rupture (especially Achilles tendon), sometimes bilateral, may occur with quinolone therapy including moxifloxacin, even within 48 hours of starting treatment and have been reported up to several months after discontinuation of therapy. The risk of tendinitis and tendon rupture is increased in elderly patients and in those treated concurrently with corticosteroids. At the first sign of pain or inflammation, patients should discontinue treatment with moxifloxacin, rest the affected limb(s) and consult their doctor immediately in order to initiate appropriate treatment (e.g. immobilisation) for the affected tendon.
Patients should be advised to avoid exposure to either UV irradiation or extensive and/or strong sunlight during treatment with Moxispey.
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.
Moxispey solution for infusion is for intravenous administration only. Intra-arterial administration should be avoided since preclinical studies demonstrated peri-arterial tissue inflammation following infusion by this route.
Moxispey therapy may interfere with the Mycobacterium spp. culture test by suppression of mycobacterial growth causing false negative results in samples taken from patients currently receiving moxifloxacin. Moxispey 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.
Effects on ability to drive and use machines:
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.
Presentation:
100 ml LDPE bottles pack in carton along with leaflet.
Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescription only medicine (POM).