APPROVED
The Order of the Ministry
of Health of Ukraine
03.11.2016 No.1166
Registration Certificate
No.UA/5050/01/01

УТВЕРЖДЕНО
Приказ Министерства
здравоохранения Украины
03.11.2016 №1166
Регистрационное удостоверение
№UA/5050/01/01

INSTRUCTION
for medical use of medicinal product
LEKCIN®

ИНСТРУКЦИЯ
по медицинскому применению
лекарственного средства
ОФЛОКСАЦИН
(OFLOXACIN)

Composition:
active ingredient: ofloxacin;
1 tablet contains ofloxacin 200 mg;
excipients: lactose monohydrate; potato starch; magnesium stearate; stearic acid; croscarmellose sodium.

Pharmaceutical form. Tablets.
Main physicochemical properties: yellowish-white tablets.

Pharmacotherapeutic group. Antibacterials for systemic use. Quinolone antibacterials. Ofloxacin. ATC Code J01M A01.

Pharmacological properties.
Pharmacodynamics. The drug is a fluoroquinolone antimicrobial with broad-spectrum activity. Bactericidal effect of ofloxacin is conditioned by its ability to inhibit the bacterial enzyme, DNA gyrase, thus disturbing function of bacterial DNA. The range of antimicrobial action of ofloxacin involves most gram-negative and some gram-positive microorganisms. The following causative microorganisms are susceptible to ofloxacin: *Staphylococcus aureus* (including methicillin-resistant staphylococci), *Staphylococcus epidermidis, Neisseria gonorrhoeae; Neisseria meningitides; Escherichia coli; Salmonella spp.; Shigella spp.; Morganella morganii, Yersinia spp.; Haemophilus influenzae; Citrobacter;, Klebsiella oxytoca; Enterobacter, Hafnia; Proteus* (indol-positive and indol-negative species); *Campilobacter jejuni, Aeromonas hydrophilia; Plesiomonas; Vibrio cholerae; Vibrio parahaemolyticus; Chlamidia; Legionella; Helicobacter pylori* and aerobic gram-positive bacteria – staphiloccoci, including penicillinase-producing strains.
Intermediately susceptible: *Enterococcus; Streptococcus (S. pyogenes, S. pneumoniae, S. viridans); Serratia marcescens; Acinetobacter; Mycoplasma hominis; Mycoplasma pneumoniae; Pseudomonas aeruginosa*; mycobacterium tuberculosis and *Mycobacterium fortuitum.*
A synergic effect of ofloxacin and rifabutin on *Mycobacterium leprae* was established.
Mostly resistant: anaerobic bacteria *(Bacteriodes, Peptococcus, Peptostreptococcus, Eubacterium, Fusobacterium, Clostridium difficile); Ureaplasma urealyticum, Nocardia asteroids.*
Ineffective for *Treponema pallidum.*
Pharmacokinetics.
Internal use of the product is followed by rapid and easy absorption from the gastrointestinal tract (GIT). The peak plasma concentration after a single oral dose of 200 mg ofloxacin is 2.5-3 mg/mL and is attained 1-2 hours following administration. The bioavailability of the drug is 96-100%. Plasma protein binding is about 25%. Ofloxacin crosses placental barrier and is excreted into breast milk. Ofloxacin is up to 5% metabolized. The half-life of ofloxacin is 5-8 hours. Up to 80% of ofloxacin is eliminated via the kidneys as unchanged substance. Patients with renal and hepatic diseases may have prolonged elimination half-life of ofloxacin.
Following single oral dose of ofloxacin prolonged elimination half-life was established in elderly patients, peak plasma concentration being unchanged. In patients with renal failure half-life period is increased proportional to creatinine clearance, and total clearance and renal clearance are reduced.

Clinical particulars.

Indications.

Infectious and inflammatory diseases caused by ofloxacin-susceptible strains of microorganisms:
– exacerbation of chronic bronchitis and chronic obstructive pulmonary disease;
– community-acquired pneumonia;
– pyelonephritis;
– complicated and uncomplicated urinary tract infections;
– non-gonococcal/gonococcal urethritis and cervicitis;
– complicated infections of the skin and soft tissues.
The medicinal product is used to treat the above infections only when the use of other antibacterials usually prescribed for primary treatment of such infections is impossible.
Official recommendations for the proper use of antibacterials must be considered.

Contraindications.

– Hypersensitivity to the active substance and other components of the medicinal products or to other fluoroquinolones;
– Epilepsy, central nervous system lesions with lowered seizure threshold (following traumatic brain injury, stroke, inflammatory processes in the brain and meninges);
– A history of tendonitis;
– Glucose-6-phosphate dehydrogenase deficiency;
Ofloxacin should not be used in patients with prolonged QT interval, uncompensated hypoglycaemia, and in patients taking concomitantly medicinal products with known ability to prolong QT interval (class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics).

Interactions with other medicinal products and other forms of interaction

The following interactions are possible in case of concomitant use of ofloxacin with other medicinal products:
In case of concomitant use with warfarin or its derivatives prothrombin time should be controlled or other required tests need to be performed to check blood coagulation condition;
medicinal products known to prolong QT interval (e.g. Class IA and III, tricyclic antidepressants, macrolides, antipsychotics) – additional prolongation of QT interval; concomitant use is contraindicated;
antacids, sucralfate, metal cations – co-administered magnesium/aluminum antacids, sucralfate, zinc or iron preparations and can reduce absorption of ofloxacin. Therefore, ofloxacin should be taken 2 hours before such preparations;
non-steroidal anti-inflammatory drugs, medicinal products known to lower seizure threshold (e.g. theophylline) – additional lowering of the cerebral seizure threshold may occur; in case of seizures ofloxacin should be discontinued. Unlike other fluoroquinolones ofloxacin is believed not to pharmacokinetically interact with theophylline.
glibenclamide – slight elevation of plasma glibenclamide levels when administered concurrently, it is therefore recommended that patients treated with this combination be monitored particularly closely;
antidiabetic drugs – blood glucose fluctuations (hypo- or hyperglycaemia); in case of concomitant use constant monitoring of blood glucose is recommended;
indirect anticoagulants – prolonged bleeding time; in case of concomitant administration coagulation profile must be closely monitored;
medicinal products eliminated via tubular secretion (e.g. probenecid, cimetidine, furosemide, methotrexate) – elimination disorder and elevated ofloxacin plasma levels.
interference with laboratory tests – in patients treated with ofloxacin, determination of opiates or porphyrin levels in urine may give false-positive results. It may be necessary to confirm positive opiate or porphyrin screens by more specific methods.
vitamin K antagonists – coagulation tests should, therefore, be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.
Ofloxacin may inhibit growth of *Mycobacterium tuberculosis* and give false-positive results in bacteriological tests for diagnosing tuberculosis.

If high doses of the medicinal products are used its increased plasma concentration is possible.
Concomitant use of ofloxacin and caffeine, theophylline, cimetidine, cyclosporine, oral anticoagulants and drugs metabolized with participation of cytochrome P450, intensification of side effects is possible.

Special warnings and precautions for use.

Ofloxacin must be avoided in patients with a history of serious side effects with the use of fluoroquinolones (see Undesirable effects). Such patients must be treated with ofloxacin only in absence of alternative treatment options and after a thorough consideration of benefit-risk balance (see also Contraindications).
Alcohol should be avoided during the treatment.
Patients with a history of severe undesirable reactions (tendinitis, severe neurological reactions) to other quinolones are at high risk of such reactions to ofloxacin.
Care must be exerted in patients with CNS diseases (expressed cerebral atherosclerosis, history of acute cerebral circulation failure), renal impairment. Patients must be adequately hydrated to avoid crystalluria.
Dose and time of administration must be adjusted in patients with renal failure and elderly patients due to prolonged elimination half-life.
Ofloxacin is not a drug of first choice for treatment of pneumonia caused by pneumococci or mycoplasmas or acute tonsilitis caused by β-haemolytic streptococci.
Allergic and hypersensitivity reactions were reported following the use of initial dose of fluoroquinolones. Anaphylactic and anaphylactoid reactions may progress up to shock, which is life-threatening, even following the initial dose. In such cases ofloxacin must be discontinued immediately and the required therapy must be instituted immediately (e.g. shock therapy).
Prolonged, disabling and potentially irreversible serious adverse drug reactions.
Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving fluoroquinolones irrespective of their age. Ofloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their doctor for advice.
Diseases caused by Clostridium difficile.
Diarrhoea, especially if severe, persistent and/or bloody, occurring during or after treatment with ofloxacin, may indicate pseudomembranous colitis. If pseudomembraneous colitis is suspected, treatment should be discontinued immediately. Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Medicinal products that inhibit peristalsis are contraindicated in such cases.
Patients predisposed to seizures.
In case of seizures ofloxacin mut be discontinued.
QT interval prolongation.
Very rare cases of QT interval prolongation have been reported in patients taking fluoroquinolones. Caution should be taken when using fluoroquinolones, including ofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example.
– elderly patients;
– uncorrected electrolyte imbalance (hypokalaemia, hypomagnesaemia);
– congenital long QT syndrome;
– acquired long QT syndrome;
– cardiac diseases (e.g., heart failure, myocardial infarction, bradycardia).
It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment.
Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population.
Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's

disease, hypertension, known atherosclerosis).
In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.
Tendinitis and tendon rupture.
Tendinitis is rarely possible with ofloxacin therapy, which may lead to tendon rupture, including Achilles tendon. Tendinitis and tendon rupture, sometimes bilateral, may occur as early as within 48 hours of starting treatment with ofloxacin and even several months following ofloxacin discontinuation.
The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided. In case of first signs of tendinitis (e.g., edema, inflammation) ofloxacin must be discontinued immediately and respective therapeutic measures for the damaged tendon (e.g. immobilization) must be instituted.
Patients with history of psychotic disorder.
Psychotic reactions have been reported in patients receiving fluoroquinolones. In some cases these have progressed to suicidal thoughts or self-endangering behaviour including suicide attempt, sometimes after a single dose of ofloxacin. In the event that a patient develops these reactions, ofloxacin should be discontinued and appropriate measures instituted. Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.
Patients with impaired liver function.
Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur. Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.
Patients treated with vitamin K antagonists.
Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including ofloxacin, in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these drugs are given concomitantly.
Myasthenia gravis.
Ofloxacin should be administered with care in patients with a history of myasthenia gravis.
The use of antibiotics, especially if prolonged, may result in overgrowth of non-susceptible organisms, which is why patient’s condition should be monitored periodically during treatment. If secondary infection occurs during therapy, appropriate measures should be taken.
Fluoroquinolones, including ofloxacin, have neuromuscular blocking activity and may exacerbate
Peripheral neuropathy.
Cases of sensory or peripheral sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving fluoroquinolones, including ofloxacin. Patients under treatment with ofloxacin 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 (see Undesirable effects).
Hypoglycaemia.
As with all quinolones, cases of hypoglycaemia, usually in patients with diabetes mellitus treated with hypoglycaemic agents (e.g. glibenclamide) or insulin were reported. In such patients with diabetes mellitus close monitoring of blood glucose level is recommended.
Patients with glucose-6-phosphate-dehydrogenase deficiency.
Patients with latent or diagnosed glucose-6-phosphate-dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. Therefore, a special care should be exerted when administering ofloxacin to this group of patients.
Patients with rare hereditary disorders.
Patients with such rare hereditary disorders as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should restrain from using this medicinal product.

Pregnancy and lactation.

Ofloxacin is contraindicated during pregnancy.
Women are recommended to stop breast-feeding during treatment with ofloxacin.

Effects on ability to drive and use machines.

The patients should restrain from activity requiring increased attention and quick psychomotor reactions (e.g., driving) when taking ofloxacin.

Posology and method of administration.

Medicinal product is intended for internal use. Tablets must be taken with liquid. The interval between doses of ofloxacin and sucralfate, zinc and iron preparations, aluminium/magnesium-containing antacids must be at least 2 hours, as concomitant use can result in reduced absorption of ofloxacin.

Dosage.

The dose of ofloxacin is determined by the type and severity of the infection. The dosage range for adults is 200 mg to 800 mg daily. Up to 400 mg may be given as a single dose, preferably in the morning, while higher doses should be taken in two equal doses at approximately equal intervals.

Exacerbation of chronic bronchitis and chronic obstructive pulmonary disease, community-acquired pneumonia: 400 mg once a day, increasing if necessary, to 400 mg twice a day.

Complicated and uncomplicated urinary tract infections, pyelonephritis: 200-400 mg once a day, increasing if necessary, to 400 mg twice a day.

Complicated skin and soft tissue infections: 400 mg twice a day.

Uncomplicated gonococcal urethritis and cervicitis: 400 mg as a single dose. course dose – 400 mg.

Non-gonococcal urethritis and cervicitis: 400 mg a day in 1 or 2 doses.

Patients with renal impairment.

The medicinal product is used at a usual initial dose but further doses must be reduced as determined by creatinine clearance:

Creatinine clearance (Creatinine plasma level)	*Initial dose*	*Maintenance doses*
20-50 mL/min (C_{cr} – 1.5-5 mg/dL)	Usual	100*-200 mg/day
<20 mL/min (C_{cr} –>5 mg/dL)	Usual	100 mg* every 24 hours
Haemodialysis/ peritoneal dialysis	usual	100 mg* every 24 hours

*according to indication or dose interval

Patients with impaired liver function.

The excretion of ofloxacin may be reduced in patients with severe hepatic dysfunction. Therefore, it is recommended that the dose should not exceed 400 mg ofloxacin daily.

Elderly patients

No adjustment of dosage is required in the elderly other than that imposed by consideration of renal or hepatic function.

Duration

The duration of treatment depends on the severity of infection and patient's response to therapy. Usually, treatment course is 5-10 days, except of cases of uncomplicated gonorrhoea, when a single dose of 400 mg of preparation is recommended.

Treatment should not exceed 2 months duration.

Paediatric population

The medicinal product is not used in children.

Overdose

Symptoms. The most important signs to be expected following acute overdose are CNS symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures, as well as gastrointestinal reactions such as nausea and mucosal erosions.

Management. In the case of overdose steps to remove any unabsorbed ofloxacin e.g. gastric lavage, administration of adsorbants and sodium sulphate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa.

Elimination of ofloxacin may be increased by forced diuresis.

ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.

Undesirable effects.

Infections and infestations: superinfection, secondary infections (including mycoses), pathogen resistance.

Blood and lymphatic system disorders: anaemia, haemolytic anaemia, leukopenia, neutropenia, eosinophilia, thrombocytopenia, agranulocytosis, haematopoiesis suppression in the bone marrow (disappearing following drug discontinuation), pancytopenia. Splinter haemorrhages (petechiae) and nasal bleedings are possible.
Immune system, skin and subcutaneous tissue disorders: hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, angioedema, anaphylactic/anaphylactoid shock, rash (including pustulous, haemorrhagic), pruritis, urticaria, hot flushes, hyperhidrosis, erythema, Lyell's syndrome, photosensitivity reactions, drug eruption, vascular purpura, vasculitis, which can lead in exceptional cases to skin necrosis, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis, drug rash, exfoliative dermatitis, skin hyperpigmentation, changes in nail colour and nail delamination.
Metabolism and nutrition disorders: hyperglycaemia, hypoglycaemia in diabetics treated with hypoglycaemic agent, elevated plasma triglycerides, cholesterol and potassium, acidosis.
Psychiatric disorders:* agitation, sleep disorders, insomnia, psychotic disorders (including hallucinations, paranoia, maniac thoughts), anxiety, confusion, nightmares, depression, psychotic disorders and depression with self-endangering behaviour, including suicidal thoughts or suicide attempts; euphoria, phobias, irritability, anxiety, spatial disorientation.
Nervous system disorders:* headache, drowsiness, paraesthesia, dysgeusia, parosmia, peripheral sensory neuropathy, peripheral sensory motor neuropathy, convulsions, aggravation of myasthenia, extra-pyramidal symptoms or other disorders of muscular coordination, epileptic seizures, ataxia, tremor, reduced reaction rate, increased intracranial pressure, vertigo.
Eye disorders:* eye mucosa irritation, conjunctivitis, nystagmus, reduced visual acuity, visual disturbance (including diplopy, photophobia), colour blindness.
Ear and labyrinth disorders:* dizziness, tinnitus, impaired hearing, hearing loss, coordination disorders.
Cardiovascular disorders: tachycardia, arterial hypertension, ventricular arrhythmias, torsades de pointes (reported predominantly in patients with risk factors for QT prolongation); ECG QT prolonged, arterial hypertension, cerebral thrombosis, heart arrest, shock.
Respiratory, thoracic and mediastinal disorders: cough, nasopharyngitis, dyspnoea, bronchospasm, allergic pneumonitis, rhinorrhoea, wheezing, allergic pulmonitis, feeling short of breath, respiratory arrest, dyspnoea, severe dyspnoea.
Gastrointestinal disorders: anorexia, abdominal pain, nausea, vomiting, diarrhoea, enterocolitis (sometimes haemorrhagic), pseudomembranous colitis, dry mouth or burning in the mouth, dyspepsia, heartburn, flatulence, constipation, intestinal colic, intestinal perforation, intestinal bleeding.
Hepatobiliary disorders: elevated plasma levels of hepatic enzymes and bilirubin, jaundice (including cholestatic, parenchymatous), hepatitis, necrosis.
Musculoskeletal and connective tissue disorders:* tendinitis, arthralgia, myalgia, tendon ruptures (including Achilles rupture), which may occur within 48 hours of treatment start and may be bilateral, rhabdomyolysis and/or myopathy, muscular weakness, muscular cramps, muscle tear, muscle rupture, tendon pain.
Urinary disorders: elevated plasma creatinine, acute renal failure, acute interstitial nephritis, polyuria, dysuria, anuria, frequent urination, urine retention, haematuria, albuminuria, candiduria, renal calculi formation.
Genital and mammary disorders: irritation, burning and painful rash on the outer genitals in women. Vaginitis, dysmenorrhea, hypermenorrhoea, metrorrhagia are possible.
Congenital, familial and genetic disorders: acute attacks of porphyria in patients with porphyria.
Other:* general weakness, increased fatigability, malaise, asthenia, edema (including pulmonary edema), back pain, increased body temperature, chills, increased tenderness, weight loss, taste and olfactory disorders
* Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendinitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pre-existing risk factors (see Special warnings and precautions for use).

Shelf life. 3 years.

Storage. Keep away from children. Store in original package at the temperature not exceeding 25 °C.

Package. 10 tablets in a blister; 1 blister in a pack.

Prescription status. By prescription.

Manufacturer. Joint Stock Company «Lekhim-Kharkiv».

Location. Ukraine, 61115, Kharkiv region, Kharkiv, Severyna Pototskoho street, building 36.

Date of last revision. 06.02.2020