FARFOLEX

Instruction for use of the drug

Trade name: Farfolex.
International Nonproprietary Name: Ofloxacin.
Dosage form: Solution for infusion.
Composition: Each 100 ml contains:
Ofloxacin BP 200 mg;
Excipients q.s.
ATC Code: J01MA01.
Pharmacotherapeutic group: Quinolone antibacterials. Fluoroquinolones.
Pharmacological action:
Pharmacodynamics:
Ofloxacin is a quinolone-carboxylic acid derivative with a wide range of antibacterial activity against both Gram-negative and Gram-positive organisms. It inhibits bacterial DNA replication by blocking DNA topo-isomerases, in particular DNA gyrase.
Antimicrobial spectrum includes *Gram-positive aerobes:* Staphylococcus aureus (meticillin-susceptible), Staphylococcus epidermidis (meticillin-susceptible), Staphylococcus saprophyticus, Streptococcus pneumoniae (penicillin-susceptible), Streptococcus pyogenes.
Gram-negative aerobes: Acinetobacter calcoaceticus, Bordetella pertussis, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus ducreyi, Haemophilus influenzae, Klebsiella oxytoca, Moraxella catarrhalis, Morganella morganii, Klebsiella pneumoniae, Neisseria gonorrhoeae, Proteus mirabilis, Proteus vulgaris , Providencia rettgeri, Providencia stuartii, Pseudomonas aeruginosa (quickly develop resistance), Serratia marcescens.
Anaerobic bacteria: Clostridium perfringens.
Other: Chlamydia trachomatis, Chlamydia pneumoniae, Gardnerella vaginalis, Legionella pneumophlia, Mycoplasma hominis, Mycoplasma pneumoniae, Ureaplasma urealyticum.
In most cases, insensitive: Nocardia asteroides, anaerobic bacteria (including Bacteroides spp., Peptococcus spp., Peptostreptococcus spp., Eubacterium spp., Fusobacterium spp., Clostridium difficile), Enterococcus spp., Most of Streptococcus spp., Not effect on Treponema pallidum.
Pharmacokinetics:
After a single infusion of 200 mg ofloxacin in 60 minutes Cmax is 2.7 mcg / ml , the concentrations at 12 hours after dosing is 0.3 mcg/mL.
Steady-state concentrations were attained after four doses, and the area under the curve (AUC) was approximately 40% higher than the AUC after a single dose. The mean peak and trough plasma steady-state levels attained following intravenous administration of 200 mg of ofloxacin q 12 h for seven days were 2.9 and 0.5 µg/mL, respectively.
Elimination of ofloxacin is primarily by renal excretion. Approximately 65% of a dose is excreted renally within 48 h. <5% of an administered dose is recovered in the urine as the desmethyl or N-oxide metabolites. 4-8% of an ofloxacin dose is excreted in the feces. This indicates a small degree of biliary excretion of ofloxacin.
Indications for use:
It is indicated for the treatment of the following infections when caused by sensitive organisms:
- Respiratory tract infections (acute and chronic bronchitis, pneumonia, including those caused by intracellular or atypical pathogens, with the exception of pneumococcal infections);
- Acute, chronic and recurrent infections of upper respiratory tract (except for cases of acute tonsillitis - strains as Streptococcus spp. moderately susceptible to ofloxacin, the drug should not be used as a tool of choice for the treatment of pneumonia caused by pneumococcus, and acute tonsillitis (ß-hemolytic streptococcus));
- Infections of skin and soft tissue;
- Infection of bone (osteitis, osteomyelitis) and joints;
- Abdominal infections, including infections of the biliary tract;
- Intestinal infections, including escherichiosis, salmonellosis, shigellosis, cholera, yersiniosis;
- Infectious and inflammatory diseases of the pelvic organs (pelvioperitonit, salpingitis, oophoritis, tubo-ovarian abscesses, endometritis);
- Complicated and uncomplicated infectious and inflammatory diseases of the urinary tract, prostate and urethra, including gonococcal etiology;
- Sepsis;
- Prevention of bacterial infections in patients with impaired immunity, including neutropenia.

Contra-indications:
- hypersensitivity to fluoroquinolones;
- children up to age 18;
- pregnancy, lactation;
- patients with deficiency of glucose-6-phosphate dehydrogenase;
- epileptics (including history), decrease seizure threshold (including after brain injury, stroke or inflammation of the central nervous system);
- if there are indications of damage tendons, against previously held receiving fluoroquinolones.

Application for violations of liver function: the maximum daily dose in hepatic failure - 400 mg / day.
Use in renal impairment: in patients with renal impairment (with CC from 50 to 20 ml / min) single dose should be 50% of the average dose in the multiplicity of purposes, 2 times / day. Or complete a single dose administered 1 time / day. When clearance <20 ml/min single dose - 200 mg, then - 100 mg / day, every other day.
Dosage and directions for use:
General dosage recommendations:
The dose of ofloxacin is determined by the type and severity of the infection. A daily dose of up to 400 mg ofloxacin may be given as a single dose. In this case, it is preferable to administer ofloxacin in the morning.
Daily doses of more than 400 mg must be divided into two separate doses and be given at approximately equal intervals.
Adults:
The usual intravenous dosages in adults are:
Complicated urinary tract infection: 200 mg daily.
Lower respiratory tract infection: 200 mg twice daily.
Septicaemia: 200 mg twice daily.
Skin and soft tissue infections: 400 mg twice daily.
Farfolex solution is only intended for SLOW intravenous infusion; it is administered once or twice daily. The infusion time for Farfolex IV should not be less than 30 minutes for 200 mg.
This is of particular importance when ofloxacin is administered concomitantly with drugs that can lead to a reduction in blood pressure or with barbiturate-containing anaesthetics. Generally, individual doses are to be given at approximately equal intervals.
The dose may be increased to 400 mg twice daily in severe or complicated infections.
Posology in patients with renal insufficiency:
In patients with impaired renal function, the following oral or I.V. dosages are recommended:

CREATININE CLEARANCE	UNIT DOSE mg*	NUMBER / 24 h	INTERVALS h
50 – 20 ml/min	100 – 200	1	24
< 20 ml/min** or haemodialysis or peritoneal dialysis	100 or 200	1 1	24 48

* According to indication or dose interval.
** The serum concentration of ofloxacin should be monitored in patients with severe renal impairment and dialysis patients.
Posology in hepatic insufficiency (e.g. cirrhosis with ascites)
It is recommended that a maximum daily dose of 400 mg of ofloxacin be not exceeded, because of possible reduction of excretion.
Children:
Farfolex is not indicated for use in children or growing adolescents.
Elderly:
Age in itself does not impose to adapt the dosage of Farfolex. However, special attention to renal function should be paid in elderly patients, and the dosage should be adapted accordingly.
Duration of treatment:
The duration of treatment is determined according to the response of the causative organisms and the clinical picture.
As with all antibacterial agents, treatment with Farfolex should be continued for at least 3 days after the body temperature has returned to normal and the symptoms have subsided.
In most cases of acute infection, a course of treatment lasting 7 to 10 days is sufficient. Once the patient's condition has improved, the mode of administration should be changed from parenteral to oral, normally at the same total daily dose.
Treatment should not exceed 2 months duration.
Side-effects:
Infections and infestations: Uncommon - Fungal infection, Pathogen resistance.
Blood and the lymphatic system disorders: Very rare – Anaemia, Haemolytic anaemia, Leukopenia, Eosinophilia, Thrombocytopenia. Not known – Agranulocytosis, Bone marrow failure.
Immune system disorders: Rare - Anaphylactic reaction, Anaphylactoid reaction, Angioedema. Very rare - Anaphylactic shock, Anaphylactoid shock.
Metabolism and Nutrition disorders: Rare – Anorexia. Not known - Hypoglycaemia in diabetics treated with hypoglycaemic agents. Hyperglycaemia, Hypoglycaemic coma.
Psychiatric disorders: Uncommon - Agitation, Sleep disorder, Insomnia. Rare - Psychotic disorder (for e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression. Not known - Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt, Nervousness.
Nervous system disorders: Uncommon - Dizziness, Headache. Rare- Somnolence, Paraesthesia, Dysgeusia, Parosmia. Very rare - Peripheral sensory neuropathy, Peripheral sensory motor neuropathy, Convulsion, Extra-pyramidal symptoms or other disorders of muscular coordination. Not known - Tremor, Dyskinesia, Ageusia Syncope.
Eye disorders: Uncommon - Eye irritation. Rare - Visual disturbance.
Ear and labyrinth disorders: Uncommon - Vertigo. Very rare - Tinnitus, Hearing loss. Not known - Hearing impaired.
Vascular disorders: Common – Phlebitis. Rare – Hypotension. Not known - During infusion of ofloxacin, tachycardia and hypotension may occur. Such a decrease in blood pressure may, in very rare cases, be severe.
Respiratory, thoracic and mediastinal disorders: Uncommon - Cough, Naso-pharyngitis. Rare - Dyspnoea, Bronchospasm. Not known - Allergic pneumonitis, Severe dyspnoea.
Gastrointestinal disorders: Uncommon - Abdominal pain, Diarrhoea, Nausea, Vomiting. Rare - Enterocolitis, sometimes haemorrhagic. Very rare - Pseudomembranous colitis, Jaundice cholestatic. Not known – Dyspepsia, Flatulence, Constipation, Pancreatitis.
Hepato-bilary disorders: Rare - Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase), Blood bilirubin increased. Not known - Hepatitis, which may be severe.
Skin and subcutaneous tissue disorders: Uncommon - Pruritus, Rash. Rare - Urticaria, Hot flushes, Hyperhidrosis, Pustular rash. Very rare - Erythema multiforme, Toxic epidermal necrolysis, Photo-sensitivity reaction, Drug eruption, Vascular purpura, Vasculitis, which can lead in exceptional cases to skin necrosis. Not known - Stevens-Johnson syndrome, Acute generalized exanthemous pustulosis, drug rash Stomatitis.
Musculoskeletal and Connective tissue disorders: Rare – Tendonitis. Very rare - Arthralgia, Myalgia,
Tendon rupture (e.g. Achilles tendon) which may occur within 48 hours of treatment start and may be bilateral. Not known - Rhabdomyolysis and/or Myopathy, Muscular weakness, Muscle tear, muscle rupture, Ligament rupture, Arthritis.
Renal and Urinary disorders: Rare – Serum creatinine increased. Very rare - Acute renal failure. Not known - Acute interstitial nephritis.
Congenital and familial/genetic disorders: Not known - Attacks of porphyria in patients with porphyria.
General disorders and administration site conditions: Common - Infusion site reaction (pain, reddening). Not known - Asthenia Pyrexia Pain (including pain in the back, chest and extremities).
Overdose:
Symptoms: CNS symptoms such as confusion, dizziness, impairment of consciousness and seizures, increases QT interval as well as gastrointestinal reactions such as nausea and mucosal erosions.
Treatment: Elimination of ofloxacin may be increased by forced diuresis. In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. Antacids may be used for protection of gastric mucosa.
A fraction of ofloxacin may be removed from the body with haemodialysis. Peritoneal dialysis and CAPD are not effective in removing ofloxacin from the body. No specific antidote exists.
Drug Interactions:
Drugs known to prolong QT interval:
Ofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
Prolongation of bleeding time has been reported during concomitant administration of ofloxacin and anticoagulants.
Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs:
No pharmacokinetic interactions of ofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal anti-inflammatory drugs, or other agents, which lower the seizure threshold.
In case of convulsive seizures, treatment with ofloxacin should be discontinued.
Glibenclamide:
Ofloxacin may cause a slight increase in serum concentrations of glibenclamide administered concurrently; patients treated with this combination should be closely monitored.
Probenecid, cimetidine, furosemide and methotrexate:
Caution should be exercised when ofloxacin is co-administered with drugs that affect the tubular renal secretion such as probenecid, cimetidine, furosemide and methotrexate.
Vitamin K antagonists:
Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with ofloxacin in combination with a vitamin K antagonist (e.g. warfarin) .Coagulation tests should be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.
Cautions:
Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin (including several weeks after treatment), may be symptomatic of pseudo-membranous colitis (CDAD). CDAD may range in severity from mild to life threatening, the most severe form which is pseudomembranous colitis. It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with ofloxacin .If pseudo-membranous colitis is suspected, ofloxacin must be stopped immediately.
Should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.
Farfolex is not recommended in patients with a known history of myasthenia gravis.
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 and for 48 hours following treatment discontinuation in order to prevent photosensitisation.
Farfolex should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.
In diabetic patients, careful monitoring of blood glucose is recommended.
If Farfolex has to be used in patients with glucose-6-phosphate-dehydrogenase deficiency, potential occurrence of haemolysis should be monitored.
In patients treated with Farfolex, determination of opiates in urine may give false-positive results. It may be necessary to confirm positive opiate screens by more specific method.
Patients with rare hereditary disorders of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Effects on ability to drive and use machines:
Since there have been occasional reports of somnolence, impairment of skills, dizziness and visual disturbances, patients should know how they react to Farfolex before they drive or operate machinery.
Presentation:
1X1, 100 ml FFS Plastic bottle in a monocarton, with instruction for use.
Storage:
Keep in dry place protected from light at a temperature below 30°C. Keep out of reach of children. Do not freeze.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescription only medicine (POM).

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Manufactured for:
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