Ofloxacin

Inoflox®

200 & 400 mg Tablet • 200 mg/100 mL Solution for Infusion
Antibacterial (Fluoroquinolone)

FORMULATIONS
Each film-coated tablet contains:
Ofloxacin ..... 200 mg or 400 mg

Each 100 mL solution contains:
Ofloxacin ..... 200 mg

PRODUCT DESCRIPTIONS
Ofloxacin (Inoflox®) 200 mg tablet is a beige, standard biconvex film-coated tablet, bisected on one side and plain on the other side.

Ofloxacin (Inoflox®) 400 mg tablet is a beige, round film-coated tablet, bisected on one side and plain on the other side.

Ofloxacin (Inoflox®) 200 mg/100 mL solution for infusion is a clear, greenish-yellow solution, free from extraneous matter with a pH of 4-5. It is contained in a 100 mL type I glass vial with chlorobutyl gray rubber stopper with green flip-off seal.

PHARMACODYNAMICS
Ofloxacin is a synthetic broad-spectrum fluoroquinolone antimicrobial agent which inhibits DNA topoisomerase, more commonly referred to as the DNA gyrase. DNA gyrase is necessary for bacterial DNA replication and some aspects of transcription, repair, recombination, and transposition. Inhibition of DNA gyrase in susceptible microorganisms results in the inhibition of ATP-dependent negative supercoiling of DNA, inhibition of ATP-independent relaxation of supercoiled DNA, and promotion of double-stranded DNA breakage resulting in bacterial cell death.

ANTIMICROBIAL SPECTRUM OF ACTIVITY
Ofloxacin is active *in vitro* and in clinical infections against most strains of the following microorganisms:

Aerobic Gram - positive	Aerobic Gram - negative
Staphylococcus aureus (methicillin - susceptible strains) *Streptococcus pneumoniae* (penicillin - susceptible strains) *Streptococcus pyogenes*	*Citrobacter koseri* *Enterobacter aerogenes* *Escherichia coli* *Haemophilus influenzae* *Klebsiella pneumoniae* *Neisseria gonorrhoeae* *Proteus mirabilis* *Pseudomonas aeruginosa** *Shigella* spp. *Salmonella typhi* *Yersinia enterocolitica*
Other Microorganisms	
Chlamydia trachomatis *Mycobacterium tuberculosis*	

*As with other drugs in this class, some strains of *Pseudomonas aeruginosa* may develop resistance fairly rapidly during treatment with ofloxacin.

Ofloxacin has been shown to be active *in vitro* against most strains of the following microorganisms; however, the clinical significance of these data is unknown:

Aerobic Gram - positive	Aerobic Gram - negative	
Staphylococcus epidermidis (methicillin - susceptible strains) *Staphylococcus saprophyticus* *Streptococcus pneumoniae* (penicillin - resistant strains)	*Acinetobacter calcoaceticus* *Bordetella pertussis* *Citrobacter freundii* *Enterobacter cloacae* *Haemophilus ducreyi* *Klebsiella oxytoca*	*Moraxella catarrhalis* *Morganella morganii* *Proteus vulgaris* *Providencia rettgeri* *Providencia stuartii* *Serratia marcescens*
Anaerobes	**Other Microorganisms**	
Clostridium perfringens	*Chlamydia pneumoniae* *Gardnerella vaginalis* *Legionella pneumophila*	*Mycoplasma hominis* *Mycoplasma pneumoniae* *Ureaplasma urealyticum*

Many strains of other streptococcal species, *Enterococcus* species, and anaerobes are resistant to ofloxacin.

It is suggested to carry out susceptibility tests.

PHARMACOKINETICS
After oral administration, maximum serum ofloxacin concentration is achieved within one to two hours with a bioavailability of about 98%. Ofloxacin absorption after a single or multiple 200 mg or 400 mg dose is predictable and the amount of drug absorbed increases proportionately with increasing dose and generally is unaffected by age. Although food slightly decreases the rate and/or extent of absorption, this drug-food interaction is not considered to be of clinical significance.

After oral administration of a single 200, 300, or 400 mg dose of ofloxacin in healthy fasting adults, peak serum concentrations (C_{max}) average 1.5-2.7, 2.4-4.6, or 2.9-5.6 mcg/mL, respectively. Some accumulation occurs following multiple doses. Steady-state serum concentrations of the drug are achieved after 4 doses and are about 40% higher than concentrations achieved after single oral doses.

The pharmacokinetics of ofloxacin after parenteral infusion are very similar to those observed after oral administration. After intravenous (IV) infusion of 200 mg ofloxacin C_{max} is 2.3±0.6 mcg/mL, and with 400 mg dose is 4.5±0.8 mcg/mL.

Ofloxacin is widely distributed into body tissues and fluids including bone, cartilage, bile, skin, sputum, bronchial secretions, pleural effusions, tonsils, saliva, gingival mucosa, nasal secretions, aqueous humor, tears, sweat, lung, blister fluid, pancreatic fluid, ascitic fluid, peritoneal fluid, gynecologic tissue, vaginal fluid, cervix, ovary, semen, prostatic fluid, and prostatic tissue. Ofloxacin concentrations in most tissues and fluids are generally 0.5 to 1.7 times higher than serum concentration. Ofloxacin also distributes into the cerebrospinal fluid (CSF) with peak concentrations attained within 2 to 6 hours after oral administration depending on the degree of inflammation. Peak CSF concentrations, like in most tissues and fluids, are higher than the drug's serum concentration.

The apparent volume of distribution is 1 to 2.5 L/kg and is generally not affected by renal impairment. About 20 to 32% is protein-bound, mainly to albumin.

Ofloxacin is primarily metabolized into desmethyl ofloxacin and ofloxacin *N*-oxide. After a single 100 mg to 600 mg oral ofloxacin dose, 65% to 90% is excreted unchanged in the urine within 48 hours while less than 5% is excreted as metabolites. About 4% to 8% is excreted in the feces.

In healthy adults with normal renal function, ofloxacin's elimination half-life is approximately 4 to 8 hours and renal clearance is about 133 to 200 mL/minute.

Hemodialysis removes only small amounts of ofloxacin and its desmethyl metabolite. After a single 100 or 200 mg ofloxacin dose, about 10% to 21% is removed by hemodialysis while 10% of a single 200 mg ofloxacin dose is removed via peritoneal dialysis.

INDICATIONS
For the treatment of the following infections caused by susceptible microorganisms:
- Acute bacterial exacerbations of chronic bronchitis
- Community-acquired pneumonia
- Uncomplicated skin and skin structure infections
- Non-gonococcal urethritis and cervicitis
- Acute pelvic inflammatory disease
- Uncomplicated cystitis
- Acute uncomplicated pyelonephritis
- Complicated urinary tract infections
- Prostatitis
- Enteric infections including typhoid fever and shigellosis

DOSAGE AND ADMINISTRATION
- Patients receiving oral or IV ofloxacin should be well hydrated to prevent formation of highly concentrated urine. Crystalluria and cylindruria have been reported with quinolones.
- Ofloxacin tablets can be taken with or without food. Administer dose at least 2 hours before or 2 hours after antacids containing magnesium or aluminum, after sucralfate or metal cations such as iron, multivitamin preparations with zinc, or didanosine (see INTERACTIONS WITH OTHER MEDICAMENTS)
- Ofloxacin solution for infusion should be administered only by slow IV infusion over a period of 30-60 minutes (see **Directions for Use, Compatibility and Stability**).

Usual Adult Oral / IV Dose: 200 mg to 400 mg every 12 hours. The dose and duration of treatment are based on the type and severity of infection being treated (see **Dosing Table**).

Recommended Oral / IV Dose for Specific Infections in Adults:

Infection	Recommended Oral /IV Ofloxacin Dose	Frequency	Duration
Acute bacterial exacerbation of chronic bronchitis	400 mg	Every 12 hours	10 days
Community-acquired pneumonia	400 mg	Every 12 hours	10 days
Uncomplicated skin and skin structure infections	400 mg	Every 12 hours	10 days
Nongonococcal cervicitis/ urethritis due to *Chlamydia trachomatis*	300 mg	Every 12 hours	7 days
Acute pelvic inflammatory disease *	400 mg	Every 12 hours	10 to 14 days
Uncomplicated cystitis due to *Escherichia coli* or *Klebsiella pneumoniae*	200 mg	Every 12 hours	3 days
Acute uncomplicated pyelonephritis	400 mg	Every 12 hours	14 days
Uncomplicated cystitis due to other susceptible pathogens	200 mg	Every 12 hours	7 days
Complicated urinary tract infections	200 mg	Every 12 hours	14 days
Prostatitis	300 mg	Every 12 hours	6 weeks
Typhoid fever	15 mg/kg/day to be given in two divided doses (Maximum total daily dose is 800 mg in two divided doses)	Every 12 hours	5 to 14 days
Shigella enteritis	400 mg	Single dose	–
	200 mg	Every 8 hours	1 day
· 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.			

*With or without an anti-infective active against anaerobes, e.g., metronidazole 500 mg twice a day for 14 days (see respective product label for prescribing information).

Patients with Renal Impairment: Doses and/or frequency of ofloxacin administration should be decreased in patients with creatinine clearances of 50 mL/minute or less. After a normal initial dose (see **Usual Adult Dose**), the dose should be adjusted as follows:

Creatinine Clearance (mL/min)	Oral /IV Maintenance Dose	Frequency
20 to 50	. Give the usual recommended dose	Every 24 hours
< 20	Give ½ of the usual recommended dose	Every 24 hours

When only the serum creatinine value is available, the following formula may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

$$\text{Men: } CL_{cr}\ (\text{mL/min}) = \frac{\text{Weight (kg) x (140 age in years)}}{72 \times \text{serum creatinine (mg/dL)}}$$

Women: 0.85 x value calculated using the above formula

Patients with Hepatic Impairment: The excretion of ofloxacin may be reduced in patients with severe liver function disorders (e.g., cirrhosis with or without ascites). A maximum dose of 400 mg per day should therefore not be exceeded.

Or, as prescribed by a physician.

Directions for Use, Compatibility and Stability:
- Prior to administration, parenteral drug products should be inspected visually for particulate matter and discoloration whenever solution and container permit.
- Ofloxacin solution for infusion should be used as soon as the vial is opened.
- Observe strict aseptic technique when inserting the cannula of the infusion set into the spout of ofloxacin solution for infusion. If contaminated, it has the potential to become a source of infection to patients. The cannula of the infusion set should be inserted fully and not halfway into the spout of the ofloxacin solution for infusion container to avoid leakage.
- Ofloxacin solution for infusion is compatible with isotonic saline solution, Ringer's solution and Dextrose 5% solution.
- Ofloxacin solution for infusion is incompatible with heparin.

CONTRAINDICATIONS
- Known hypersensitivity to ofloxacin, other quinolones, or to any component of the product.
- Epileptics as well as patients with lowered cerebral seizure threshold due to preexisting central nervous system (CNS) lesions, e.g., after cerebrocranial injuries, inflammations in the region of the CNS, or stroke

WARNINGS AND PRECAUTIONS

Fluoroquinolones, including ofloxacin, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk 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.

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

Tendinopathy and Tendon Rupture: Fluoroquinolones including ofloxacin, 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. This risk is further increased in those over 60 years old, in kidney, heart, or lung transplant recipients, and with concomitant steroid therapy. Strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis may also increase the risk of tendon rupture. Tendinitis and tendon rupture have been reported 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. Ofloxacin 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 doctor about changing to a non-quinolone antimicrobial drug.

Myasthenia gravis: Fluoroquinolones, including ofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis. Post-marketing serious adverse events, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in persons with myasthenia gravis. Ofloxacin should be avoided in patients with known history of myasthenia gravis.

The safety and efficacy of ofloxacin in pediatric patients, adolescents (under 18 years old), pregnant women, and breastfeeding women have not been established.

In immature rats, oral ofloxacin dosages 5 to 16 times the usual human dose increased the incidence and severity of osteochondrosis and lesions were still present and had not regressed even after 13 weeks of drug discontinuation. Studies in various species of immature animals also showed that ofloxacin and other fluoroquinolones can cause erosion of the cartilage in weight-bearing joints and other signs of arthropathies.

Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving fluoroquinolones, including ofloxacin. These reactions often occur after the first dose. Some reactions have been accompanied by cardiovascular collapse, hypotension/shock, seizure, loss of consciousness, tingling, angioedema (including tongue, larynx, throat, or facial edema/swelling), airway obstruction (including bronchospasm, shortness of breath and acute respiratory distress), dyspnea, urticaria, itching, and other serious skin reactions.

Serious acute hypersensitivity reactions may require treatment with epinephrine and other resuscitative measures, including oxygen, IV fluids, antihistamines, corticosteroids, pressor amines, and airway management, as clinically 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 treatment with fluoroquinolones, including ofloxacin. Clinical manifestations which may be severe and generally occur after multiple doses may include one or more of the following: fever, rash or severe dermatologic reactions (e.g., 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.

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

Central Nervous System (CNS) Effects: Convulsions, toxic psychoses, increased intracranial pressure have been reported in patients receiving fluoroquinolones, including ofloxacin. Fluoroquinolones may also cause CNS stimulation which may lead to tremors, restlessness, anxiety, lightheadedness, confusion, hallucinations, paranoia, depression, nightmares, insomnia, anxiety, and rarely, suicidal thoughts or acts. These reactions may occur after the first dose. If these reactions occur in patients receiving ofloxacin, the drug should be discontinued and appropriate measures instituted. As with other fluoroquinolones, ofloxacin should be used with caution in patients with known or suspected CNS disorders (e.g., severe cerebral arteriosclerosis, epilepsy), or other risk factors (e.g., certain drug therapy, renal impairment) that may predispose to seizures or lower the seizure threshold. Ofloxacin should be used with caution in patients with unstable psychiatric illness.

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 ofloxacin. Symptoms may occur soon after initiation of ofloxacin and may be irreversible. Ofloxacin should be discontinued immediately if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, and/or weakness or other alterations of sensation including light touch, pain, temperature, position sense, and vibratory sensation.

Cardiac Disorders: Prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia have been reported in some fluoroquinolones, including ofloxacin. Rare cases of *torsades de pointes* have been spontaneously reported during post-marketing surveillance in patients receiving ofloxacin. Ofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, bradycardia, or myocardial ischemia. The risk of arrhythmias may be reduced by avoiding concomitant use with other drugs that prolong the QT interval including macrolide antibiotics, antipsychotics, tricyclic antidepressants, class IA (quinidine, procainamide) or class III (amiodarone, sotalol) antiarrhythmic agents, and cisapride. Elderly patients generally may be more susceptible to drug-associated effects on the QT interval.

Clostridium difficile-associated diarrhea (CDAD) and colitis: These have been observed with the use of nearly all antibacterial agents, including ofloxacin, and may range in severity from mild to life threatening. It is important to consider this diagnosis in patients who present with diarrhea following administration of antibacterial agents.

Blood Glucose Disturbances: As with other fluoroquinolones, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g., glibenclamide) or with insulin. Careful monitoring of blood glucose is recommended in these patients. Ofloxacin should be discontinued and appropriate therapy initiated immediately if a hypoglycemic reaction occurs.

Patients with G-6-phosphate dehydrogenase deficiency: Use with caution in patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity who may be prone to hemolytic reactions when treated with fluoroquinolones.

Photosensitivity/Phototoxicity: Moderate to severe photosensitivity/ phototoxicity reactions manifesting as exaggerated sunburn reaction have been observed in patients exposed to direct sunlight or ultraviolet (UV) light while receiving fluoroquinolones; hence, direct exposure to excessive sunlight or UV radiation should be avoided during treatment. Therapy should be discontinued if photosensitization occurs.

Crystalluria: Patients receiving ofloxacin should be well hydrated to prevent formation of highly concentrated urine.

OTHER PRECAUTIONS
- As with any potent antimicrobial drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during prolonged treatment.
- Prescribing ofloxacin 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.
- As with other antibacterial drugs, long term or repeated use may result in overgrowth of non-susceptible organisms, including fungi.

INTERACTIONS WITH OTHER MEDICAMENTS

DRUGS	NATURE OF INTERACTION
Antacids, Sucralfate, Didanosine, Metal Cations, Multivitamins	Concomitant administration of quinolones with antacids containing calcium, magnesium, or aluminum, as well as sucralfate, didanosine, metal cations such as iron, or multivitamin preparations with zinc, may interfere with the GI absorption of quinolones resulting in systemic levels considerably lower than desired. These agents should be taken at least two hours before or two hours after ofloxacin therapy.
Antidiabetic agents	Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with quinolones and an antidiabetic agent. Careful monitoring of blood glucose is recommended when these agents are co-administered.
Aminoglycosides	There may be additive or partially synergistic *in vitro* activity between ofloxacin and aminoglycosides (e.g., amikacin, gentamicin, netilmicin, tobramycin) against *Pseudomonas aeruginosa or Escherichia coli*. However, synergism between the drugs is unpredictable, and indifference or antagonism has been reported more frequently.
Antimycobacterial Agents	Ofloxacin, in combination, with aminosalicylic acid, ethambutol, ethionamide, kanamycin, isoniazid, rifampicin or streptogammin, is neither synergistic nor antagonistic against *Mycobacterium tuberculosis*. Concurrent administration of ofloxacin and ethambutol results in synergistic activity *in vitro* against *Mycobacterium avium complex* (MAC); clinical importance of this interaction has not been determined. Concomitant use of ofloxacin and cycloserine has been reported to cause insomnia and seizures in a few patients with multidrug-resistant pulmonary tuberculosis; exercise caution when the two drugs are used together. *In vitro* antagonistic activity against *Staphylococcus aureus* have been reported with the use of ofloxacin together with rifampicin.
β-Lactam antibiotics	Indifference generally occurs when ofloxacin is used concomitantly with ampicillin or nafcillin against Enterobacteriaceae or *Pseudomonas aeruginosa.* *In vitro,* the combination of ofloxacin and cefotaxime was neither synergistic nor antagonistic against Enterobacteriaceae, including *Klebsiella pneumoniae* and *Escherichia coli* that were slightly susceptible or resistant to cefotaxime. Ofloxacin used in conjunction with imipenem has been reported to be additive or synergistic *in vitro* against some strains of *Pseudomonas aeruginosa* or Enterobacteriaceae; however, these combinations generally are indifferent rather than additive or synergistic against these bacteria.
Caffeine	Interactions between ofloxacin and caffeine have not been detected.
Ciclosporin	Elevated serum levels of ciclosporin have been reported following concomitant treatment with some other quinolones. Interaction between ofloxacin and ciclosporin has not been studied.
Cimetidine and Ranitidine	Cimetidine has demonstrated interference with the elimination of some quinolones resulting in prolonged serum half-lives and AUCs of the drugs. Interaction between ofloxacin and cimetidine has not been studied. Concomitant administration of ranitidine does not appear to alter oral absorption of ofloxacin.
Corticosteroids	Risk of severe tendon disorders (e.g., tendinitis, tendon rupture) during treatment with ofloxacin may be increased in patients receiving corticosteroids, particularly in elderly patients.
Digoxin	There are no significant effects noted during concomitant therapy, therefore, no dosage adjustment is required.
Drugs that prolong QT interval	As with other quinolones, ofloxacin can prolong the QT interval and should be avoided in patients receiving class IA (e.g., quinidine, procainamide) or class III (e.g., amiodarone, sotalolol) antiarrhythmic agents, macrolides, antipsychotic agents, or tricyclic antidepressants.
Drugs that undergo renal tubular secretion	With high doses of quinolones, impairment of excretion and an increase in serum levels may occur when co-administered with other drugs that undergo renal tubular secretion (e.g., furosemide, methotrexate).
Metronidazole	*In vitro*, the antibacterial activity of ofloxacin and metronidazole is additive or indifferent against anaerobic bacteria; neither synergism nor antagonism occurs with this combination
Non-steroidal anti-inflammatory drugs (NSAIDs)	Concomitant administration of ofloxacin and fenfuben (an NSAID) resulted in an increased incidence of seizures (see **WARNINGS AND PRECAUTIONS**).
Probenecid	Concomitant administration of probenecid with certain other quinolones interferes with renal tubular secretion of the drugs.
Theophylline	As with other fluoroquinolones, concomitant administration of ofloxacin in patients receiving theophylline has resulted in higher and prolonged serum theophylline concentrations and may increase the risk of theophylline-related adverse effects. Therefore, theophylline levels should be closely monitored, and appropriate dosage adjustments made when ofloxacin is co-administered. Adverse reactions (including seizures) may occur with or without elevation in the serum theophylline level.
Warfarin	Prolongation of prothrombin time in patients stabilized on warfarin was reported after ofloxacin administration. Although the exact mechanism of this interaction is not known, it is hypothesized that this is due to the replacement of the anticoagulants from serum binding sites or by suppression of vitamin K production by intestinal bacteria. Monitoring of prothrombin time is recommended when these drugs are taken concomitantly.
Zidovudine	*In vitro* studies using ofloxacin and zidovudine indicate that zidovudine does not antagonize ofloxacin's antibacterial activity against susceptible *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Salmonella typhimurium*, or *Pseudomonas aeruginosa*. The combination of ofloxacin and zidovudine resulted in a slightly additive antibacterial effect *in vitro* against *Escherichia coli* and *Salmonella typhimurium*.

Interference with Laboratory Tests:
Some fluoroquinolones, including ofloxacin, may give false-positive urine screening results for opiates using commercially available immunoassay kits. Confirmation of positive opiate screen by more specific methods may be necessary.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
Pregnancy: (Pregnancy Category C). There are no adequate and well-controlled studies using ofloxacin in pregnant women. Since ofloxacin, as with most other fluoroquinolones, causes arthropathy in immature animals, the drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (see **WARNINGS AND PRECAUTIONS**).
Lactation: Ofloxacin is distributed in breast milk. Therefore, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother as well as the possible serious adverse effects to the infant.
Children: Quinolones, including ofloxacin, cause arthropathy and osteochondrosis in juvenile animals of several species (see **WARNINGS AND PRECAUTIONS**).
Elderly: No dosage adjustment is necessary for elderly patients with normal renal function. However, since ofloxacin is excreted by the kidneys and some elderly patients experience age-related reduction in renal function, care should be taken in dose selection and renal function monitoring is recommended.

Elderly patients are at increased risk of developing severe tendon disorders including tendon rupture, or prolonged QT interval leading to ventricular arrhythmias when being treated with a fluoroquinolone such as ofloxacin (see **WARNINGS AND PRECAUTIONS**).

Renal Impairment: Since clearance of ofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in patients with renal impairment (creatinine clearance <50 mL/min), adjustment of the dosage regimen in such patients is necessary to avoid drug accumulation (see **DOSAGE AND ADMINISTRATION**).
Hepatic Impairment: Although there is insufficient data regarding the drug's pharmacokinetics in patients with hepatic impairment, it is expected that elimination of ofloxacin may be reduced. Careful patient monitoring and appropriate laboratory studies should be performed prior to and during therapy with ofloxacin.
Effects on Ability to Drive and Use Machines: Since there is a potential for ofloxacin to cause dizziness and lightheadedness, patients should be advised to avoid performing tasks which require complete mental alertness such as driving and operating machinery until effects of drug to the individual are known.

UNDESIRABLE EFFECTS
The following adverse events were likely to be drug-related in patients receiving multiple doses of ofloxacin: nausea, insomnia, headache, dizziness, diarrhea, vomiting, rash, pruritus, external genital pruritus in women, vaginitis, and dysgeusia.

Other undesirable effects of potential medical importance have been reported in patients receiving ofloxacin, regardless of relationship to the drug:

Body as a Whole: Fatigue, asthenia, fever, chills, malaise, pain (extremities, trunk, or body as a whole)
Dermatologic/Hypersensitivity Reactions: Angioedema, pruritus, rash/pustular rash, diaphoresis, urticaria, vasculitis (which can lead in exceptional cases to skin necrosis), anaphylactic/anaphylactoid reactions (including cardiovascular collapse, shock, loss of consciousness, tingling, airway obstruction), purpura/vascular purpura, serum sickness, erythema multiforme, Stevens-Johnson syndrome, erythema nodosum, exfoliative dermatitis, hyperpigmentation, toxic epidermal necrolysis, conjunctivitis, photosensitivity/phototoxicity reaction, drug rash/vesiculobullous drug eruption, hot flushes, hyperhidrosis, acute generalized exanthematous pustulosis
Nervous System: Sleep disorders, somnolence, nervousness, convulsion/seizures, anxiety, cognitive changes, depression, dream abnormality/nightmares, euphoria, hallucinations, paresthesia, syncope, vertigo, tremor, confusion, suicidal thoughts or acts, disorientation, psychotic reactions, paranoia, toxic psychosis, phobia, agitation, restlessness, aggressiveness/hostility, manic reactions, emotional lability, peripheral neuropathy, ataxia, incoordination, dysphasia, lightheadedness, myasthenia, increased intracranial pressure; exacerbation of myasthenia gravis and extrapyramidal symptoms or other disorders of muscular coordination
Cardiovascular: Cardiac arrest, edema, hypertension, palpitations, vasodilation, chest pain, cerebral thrombosis, pulmonary edema, shock, syncope, phlebitis, prolonged QT interval leading to ventricular arrhythmias, including *torsades de pointes*; tachycardia and hypotension (which may be severe in very rare cases)
Musculoskeletal: Arthralgia, myalgia, tendinitis/tendon rupture (e.g., Achilles tendon which may occur within 48 hours of treatment and may be bilateral), weakness, rhabdomyolysis and/or myopathy; muscular weakness, muscle tear, muscle rupture
Gastrointestinal (GI): Abdominal pain/discomfort and cramps, flatulence, constipation, dry mouth, GI distress, dyspepsia, heartburn, intestinal perforation, CDAD and colitis/pseudomembranous colitis (the onset of symptoms may occur during or after antimicrobial treatment), enterocolitis (sometimes hemorrhagic), GI hemorrhage, hiccough, painful oral mucosa, pyrosis, selective effect on normal bowel flora; minimal effects on salivary flora
Nutritional/Metabolic: Decreased appetite/anorexia, thirst, weight loss, hyperglycemia, hypoglycemia
Renal: Dysuria, anuria, polyuria, increased urinary frequency; urinary retention, renal calculi, acute renal insufficiency/failure, interstitial nephritis, hematuria, albuminuria, candiduria, crystalluria, cylindruria, glucosuria, proteinuria, increased serum creatinine and blood urea nitrogen (BUN); elevated urinary pH
Hepatic: Elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase, -glutamyltransferase, alkaline phosphatase, and/or bilirubin; hepatic dysfunction including hepatic necrosis, jaundice (cholestatic or hepatocellular), hepatitis (which may be severe); hepatotoxicity/hepatic failure (including fatal cases)
Genital/Reproductive: Burning, irritation, pain, and rash of the female genitalia; dysmenorrhea, menorrhagia, metrorrhagia, vaginal candidiasis, vaginal discharge
Respiratory: Pharyngitis, respiratory arrest, cough, nasopharyngitis, rhinorrhea, dyspnea (which may be severe), bronchospasm, allergic pneumonitis, stridor
Hematologic: Anemia (including hemolytic and aplastic), hemorrhage, leukopenia, leukocytosis, neutropenia, neutrophilia, increased band forms, lymphocytopenia, eosinophilia, granulocytopenia, lymphocytosis, thrombocytopenia (including thrombotic thrombocytopenic purpura), thrombocytosis, elevated erythrocyte sedimentation rate (ESR); pancytopenia, agranulocytosis, petechiae, ecchymosis/bruising, bone marrow failure/reversible bone marrow depression; prolongation of prothrombin time; acidosis, elevation of serum triglycerides, serum cholesterol, and serum potassium
Special Senses: Blurred vision/transient visual disturbances including diplopia or changes in visual acuity or color perception; photophobia, eye irritation, nystagmus, disturbances of taste, smell (parosmia), hearing (hearing loss/decreased hearing acuity, tinnitus), and/or equilibrium, usually reversible following discontinuation
In clinical trials using multiple dose therapy, ophthalmologic abnormalities, including cataracts and multiple punctuate lenticular opacities, have been observed in patients undergoing treatment with other quinolones. However, the relationship of the drugs to these events has not been definitely established.
Other Adverse Effects: Fungal infection, epistaxis, pathogen resistance, attacks of porphyria in patients with porphyria; infusion site reaction (pain, reddening); pancreatitis, dysphagia, drowsiness, sweating, irritation at infusion site, thrombophlebitis, and acute tubular necrosis have also been reported with other quinolones

OVERDOSE AND TREATMENT
Clinical features of acute overdosage of ofloxacin may include CNS symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, as well as GI reactions such as nausea and mucosal erosions.

In the event of overdose, symptomatic treatment should be implemented. The patient should be observed and proper hydration maintained. ECG monitoring should be undertaken because of the possibility of QT interval prolongation.

Gastric lavage or induction of emesis may be used to empty the stomach. Elimination of ofloxacin may be increased by forced diuresis.

Ofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.

ADVERSE DRUG REACTION REPORTING STATEMENT
For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph AND Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

STORAGE CONDITIONS
Store at temperatures not exceeding 30°C. Protect from light.
Keep the product out of sight and reach of children.

AVAILABILITY: Ofloxacin (Inoflox®) 200 mg and 400 mg Tablet in boxes of 30's and 100's
Ofloxacin (Inoflox®) 200 mg / 100 mL Solution for Infusion, box of 1 vial

CAUTION: Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

Inoflox tablet:
Manufactured by Amherst Laboratories, Inc.
UNILAB Pharma Campus, Barangay Mamplasan
Biñan, Laguna, Philippines
for UNILAB, Inc.
No. 66 United Street, Mandaluyong City
Metro Manila, Philippines
Under license from DAIICHI SANKYO CO., LTD.
3-5-1, Nihonbashi Honcho
Chuo-ku, Tokyo, Japan

Inoflox Vial:
Manufactured by
AMHERST PARENTERALS, INC.
Sta. Rosa-Tagaytay Road, Don Jose
Sta. Rosa City, Laguna, Philippines
for UNILAB, Inc.
No. 66 United Street, Mandaluyong City
Metro Manila, Philippines
Under license from DAIICHI SANKYO CO., LTD.
3-5-1, Nihonbashi Honcho
Chuo-ku, Tokyo, Japan

Date of First Authorization:
Ofloxacin (Inoflox®) 200mg Tablet - DR-XY7575, 23 Feb 1999
Ofloxacin (Inoflox®) 400mg Tablet - DR-XY18641, 25 May 2007
Ofloxacin (Inoflox®) 200mg Solution for Infusion - DR-XY28272, 30 Jan 2003

Trusted Quality Healthcare

Date of Revision: JANUARY 2019
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Reg. IPOPHIL