Ofloxacin
Inoflox®

3 mg/mL Ophthalmic Solution
Topical Antibacterial

FORMULATION:
Each mL contains
Ofloxacin .....3 mg

PRODUCT DESCRIPTION:
Ofloxacin (Inoflox) Ophthalmic Solution is a clear, pale yellow to light yellow liquid.

CLINICAL PHARMACOLOGY:
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 supercolied DNA, and promotion of double-stranded DNA breakage resulting in bacterial cell death.
Ofloxacin, as an ophthalmic solution, has a fast bactericidal action, with 90% of most bacteria killed in 19 to 55 minutes. It also maintains an inhibitory effect on bacterial cell growth for 6 to 8 hours after drug removal.

Antimicrobial Spectrum of Activity
Ofloxacin is active *in vitro* and in clinical infections in conjunctival and/or corneal ulcer infections of the following microorganisms:

Aerobic Gram-positive	Aerobic Gram-negative
Staphylococcus aureus	*Enterobacter cloacae*
Staphylococcus epidermidis	*Haemophilus influenzae*
Streptococcus pneumoniae	*Proteus mirabilis*
Anaerobic Species	*Pseudomonas aeruginosa*
Propionibacterium acnes	*Serratia marcescens**

*Efficacy for this organism was studied in fewer than 10 infections

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

Aerobic Gram-positive	Aerobic Gram-negative
Enterococcus faecalis	*Acinetobacter calcoaceticus var. anitratus*
Listeria monocytogenes	*Acinetobacter calcoaceticus var. lwoffii*
Staphylococcus capitis	*Citrobacter diversus*
Staphylococcus hominus	*Citrobacter freundii*
Staphylococcus simulans	*Enterobacter aerogenes*
Streptococcus pyogenes	*Enterobacter agglomerans*

Aerobic Gram-positive	Aerobic Gram-negative	
	Escherichia coli	*Neisseria gonorrhoeae*
	Haemophilus parainfluenzae	*Pseudomonas acidovorans*
	Klebsiella oxytoca	*Pseudomonas fluorescens*
	Klebsiella pneumoniae	*Shigella sonnei*
	Moraxella (Branhamella) catarrhalis	
Other Microorganisms	*Moraxella lacunata*	
Chlamydia trachomatis	*Morganella morganii*	

It is suggested to carry out susceptibility tests.

Pharmacokinetics
The extent of ocular and systemic absorption of Ofloxacin following topical application to the eye has not been fully elucidated. Serum concentrations achieved after topical application to uninflamed eyes are minimal relative to those produced by oral or parenteral doses of the drug.
Ofloxacin is absorbed through the cornea into the aqueous humor following topical application to the eye; absorption is enhanced in the presence of ocular inflammation and/or epithelial defects. Following topical application to the eye of 1 drop of a 0.3% solution of Ofloxacin 4 times a day for 10.5 days in healthy women, Ofloxacin concentrations measured in tear film within 40 minutes after the final dose ranged from 5.7 to 31 mcg/g. Mean tear film levels measured 4 hours after topical administration of 9.16 mcg/g were higher than the 2 mcg/mL minimum Ofloxacin concentration necessary to inhibit 90% of most bacterial strains (MIC_{90}) *in vitro*.

Ofloxacin 0.3% solution was administered topically to humans 5 times a day for 2 days followed by 5 doses at 5 minute intervals. The mean aqueous humor concentrations were 1.2 and 1.7 mcg/mL at 60 and 120 minutes, respectively, post-instillation.

Following topical application to the eye of 2 drops of a 0.3% solution of Ofloxacin every 30 minutes beginning 4 hours before surgery in patients undergoing keratoplasty, corneal tissue, aqueous humor, and vitreous humor concentrations at the time of surgery averaged 4.4, 1.3 and 0.4 mcg/mL, respectively.

In another human study, dosing 3 times at 5 minute intervals prior to surgery resulted in mean aqueous humor concentrations of 0.5 to 0.8 mcg/mL between 30 and 180 minutes after topical administration.

Some systemic absorption of Ofloxacin occurs following topical administration to the eyes, although use of Ofloxacin ophthalmic solution to date has been associated with a low potential for causing systemic effects. Ofloxacin was detectable in serum 10 minutes after ocular administration of 1 drop of a 0.3% solution in healthy women.

Distribution of Ofloxacin into human ocular tissues and fluids following topical ophthalmic or systemic administration has not been fully characterized to date. Current information is based principally on studies in patients with uninflamed and/or uninfected eyes; distribution is likely to be greater in the presence of inflammation or infection because of disruption of the blood-ocular barrier.

Metabolism and elimination of Ofloxacin following topical administration to the eye have not been fully elucidated. Following ocular administration of 1 drop of a 0.3% solution of Ofloxacin 4 times a day for 12 doses in healthy individuals, the elimination half-life of the drug in tear film was approximately 226 minutes.

INDICATIONS:
For the treatment of external eye infections due to susceptible organisms such as in blepharitis, hordeolum, dacryocystitis, conjunctivitis, meibomitis, keratitis, trachoma, and for the prevention of infection following corneal ulceration.

For the aseptic treatment during a perioperative period for ocular surgery caused by *Staphylococcus spp., Moraxella spp., Chlamydia trachomatis, Pseudomonas spp., Haemophilus spp., Klebsiella spp., Serratia spp., Proteus spp., Acinetobacter spp., Corynebacterium spp.*, and anaerobic bacteria.

DOSAGE AND ADMINISTRATION

Adults and children 1 year and older:

Instill 1 to 2 drops three to four times a day on the affected eye(s). Continue treatment 2 days longer after the eye(s) appear normal. Do not exceed 2 weeks of application. Be careful not to touch the tip of the bottle to the eye directly in order to avoid contamination of the drug.

Discard 28 days after opening.

CONTRAINDICATIONS:
• Hypersensitivity to Ofloxacin or any other quinolone or any other component of the product

WARNINGS AND PRECAUTIONS:
• For external use for eye infections only. Ofloxacin ophthalmic solution is NOT for injection into the eye.
• Use for no longer than 2 weeks at a time. As with other anti-infective agents, prolonged use of Ofloxacin may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, discontinue Ofloxacin and institute appropriate therapy.
• Use of contact lenses is not recommended in patients receiving treatment for an eye infection.
• Ofloxacin ophthalmic solution may increase the risk of corneal perforation in those with pre-existing corneal ulcers or epithelial defects.
• Serious and occasionally fatal hypersensitivity reactions, some after the initial dose, have been reported in patients receiving systemic Ofloxacin therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (e.g., laryngeal, pharyngeal, or facial edema), airway obstruction, dyspnea, urticaria, and itching. A rare occurrence of Stevens-Johnson syndrome, which progressed to toxic epidermal necrolysis, has been reported in a patient who was receiving topical ophthalmic solution. If an allergic reaction to Ofloxacin is suspected, the patient should contact their doctor and discontinue Ofloxacin immediately. Serious acute hypersensitivity reactions may require emergency treatment. Oxygen and airway management, including intubation, should be administered as clinically indicated.
• Systemic administration of Ofloxacin at doses much higher than given or absorbed by the ophthalmic route has led to lesions or erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species.

As with other fluoroquinolones, ofloxacin should be used with caution in patients with known risk factors for prolongation of the QT interval, such as congenital long QT syndrome, concomitant use of drugs that are known to prolong the QT interval (e.g., class IA and class III antiarrhythmic agents, tricyclic antidepressants, macrolides, antipsychotics), uncorrected electrolyte imbalance (e.g., hypokalemia, hypomagnesemia), or cardiac disease (e.g., heart failure, myocardial infarction, bradycardia). Ofloxacin should be used with caution in women and elderly patients since these populations may be more susceptible to drug-associated effects on the QT interval.

INTERACTION WITH OTHER MEDICAMENTS:
Specific drug interaction studies have not been performed to date with Ofloxacin ophthalmic solution. However, since systemic absorption may occur after topical application of Ofloxacin to the eye, such as those reported with systemic administration of some quinolone anti-infectives, the possibility of drug interactions with theophylline, caffeine, oral anticoagulants, and ciclosporin should be considered.

As with other quinolones, ofloxacin can prolong the QT interval and should be avoided in patients receiving class IA (quinidine, procainamide) or class III (amiodarone, sotalol) antiarrhythmic agents, macrolides, antipsychotic agents, or tricyclic antidepressants.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
Pregnancy: Pregnancy Category C. There have been no adequate and well-controlled studies using Ofloxacin ophthalmic solution in pregnant women. Since Ofloxacin, like most other fluoroquinolones, can cause arthropathy in immature animals, Ofloxacin should not be used in pregnant women unless the benefits justify the potential risks.

Lactation: It is not known whether Ofloxacin is excreted in human milk after ophthalmic administration. Therefore, do not administer to breastfeeding women unless, in the opinion of a physician, the potential benefits of the drug justify the possible risks.

Use in children: The safety and efficacy of Ofloxacin ophthalmic solution in children younger than 1 year of age have not been established.

UNDESIRABLE EFFECTS:
The most frequent adverse effects of topical ofloxacin are transient ocular irritation or discomfort (burning, stinging, redness, itching or photophobia) following administration of the solution. Conjunctival hyperaemia, chemical conjunctivitis/ keratitis, foreign body sensation, blurred vision, periocular/facial edema, eye pain, tearing, dryness, hyperglycemia and hypoglycemia have also been reported. Dizziness with numbness and nausea, headache, toxic epidermal necrolysis, and hemorrhagic conjunctivitis with palpebral edema has been reported rarely.

Since systemic absorption may occur following topical administration of ofloxacin, the possibility of adverse systemic effects exists. Ofloxacin used systemically has rarely been associated with serious side effects. Serious reactions reported for systemic dosing of ofloxacin include convulsions and increased intracranial pressure. For the oral dosage form of ofloxacin, gastrointestinal symptoms, mainly nausea/vomiting, abdominal pain/discomfort, diarrhea and anorexia, were reported most frequently, followed by dizziness and headache, and dermatological or hypersensitivity reactions. Additional effects seen with systemic dosing of ofloxacin and other fluoroquinolones include prolonged QT interval leading to ventricular arrhythmias, *torsades de pointes*,exacerbation of myasthenia gravis symptoms, tendinitis, and tendon rupture.

OVERDOSE AND TREATMENT:
Currently, there is no information available on overdosage of Ofloxacin ophthalmic solution in humans. Overdosage following oral ingestion of the commercially available ophthalmic solution is unlikely given the limited amount of Ofloxacin present in the solution.

In the event of a topical overdosage, flush the eye with a topical ocular irrigant. In the event of accidental ingestion of 10 mL of Ofloxacin ophthalmic solution, only 30 mg of Ofloxacin would be ingested. Although this amount does not appear to be clinically significant in terms of overdosage, there could be an increased potential for systemic reactions. Immediate consultation with a physician is highly recommended.

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:
• Keep the product out of reach and sight of children
• Store at temperatures not exceeding 30°C
• Always keep bottle tightly capped. Protect from light.

Trusted Quality Healthcare

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

AVAILABILITY:
Plastic bottle of 5 mL Ophthalmic Drops

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Reg. IPOPHIL

Manufactured by
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