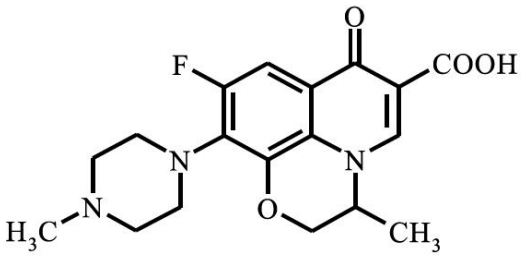
OFLOXACIN - ofloxacin solution
Rising Pharma Holdings, Inc.

Ofloxacin Ophthalmic solution USP 0.3%

DESCRIPTION

Ofloxacin ophthalmic solution 0.3% is a sterile ophthalmic solution. It is a fluorinated carboxyquinolone anti-infective for topical ophthalmic use.

Chemical Name: (±)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H* pyrido [1,2,3-*de*]-1,4 benzoxazine-6-carboxylic acid.



$C_{18}H_{20}FN_3O_4$ Mol.Wt. 361.37

Image

Contains: Active: ofloxacin 0.3% (3 mg/mL)

Preservative: benzalkonium chloride (0.005%)

Inactives: sodium chloride and water for injection. May also contain hydrochloric acid and/or sodium hydroxide to adjust pH.

Ofloxacin ophthalmic solution is unbuffered and formulated with a pH of 6.4 (range 6.0 to 6.8). It has an osmolality of 300 mOsm/kg. Ofloxacin is a fluorinated 4-quinolone which differs from other fluorinated 4-quinolones in that there is a six member (pyridobenzoxazine) ring from positions 1 to 8 of the basic ring structure.

CLINICAL PHARMACOLOGY

Pharmacokinetics:

Serum, urine and tear concentrations of ofloxacin were measured in 30 healthy women at various time points during a ten-day course of treatment with ofloxacin ophthalmic solution. The mean serum ofloxacin concentration ranged from 0.4 ng/mL to 1.9 ng/mL. Maximum ofloxacin concentration increased from 1.1 ng/mL on day one to 1.9 ng/mL on day 11 after QID dosing for 10 1/2 days. Maximum serum ofloxacin concentrations after ten days of topical ophthalmic dosing were more than 1000 times lower than those reported after standard oral doses of ofloxacin.

Tear ofloxacin concentrations ranged from 5.7 to 31 mcg/g during the 40 minute period following the last dose on day 11. Mean tear concentration measured four hours after topical ophthalmic dosing was 9.2 mcg/g.

Corneal tissue concentrations of 4.4 mcg/mL were observed four hours after beginning topical ocular application of two drops of ofloxacin ophthalmic solution every 30 minutes. Ofloxacin was excreted in the urine primarily unmodified.

Microbiology:

Ofloxacin has *in vitro* activity against a broad range of gram-positive and gram-negative aerobic and anaerobic bacteria. Ofloxacin is bactericidal at concentrations equal to or slightly greater than inhibitory concentrations. Ofloxacin is thought to exert a bactericidal effect on susceptible bacterial cells by inhibiting DNA gyrase, an essential bacterial enzyme which is a critical catalyst in the duplication, transcription, and repair of bacterial DNA.

Cross-resistance has been observed between ofloxacin and other fluoroquinolones. There is generally no cross-resistance between ofloxacin and other classes of antibacterial agents such as beta-lactams or aminoglycosides.

Ofloxacin has been shown to be active against most strains of the following organisms both *in vitro* and clinically, in conjunctival and/or corneal ulcer infections (see Indications and Usage)

AEROBES, GRAM-POSITIVE:	**AEROBES, GRAM-NEGATIVE:**
Staphylococcus aureus	*Enterobacter cloacae*
Staphylococcus epidermidis	*Haemophilus influenza*
Streptococcus pneumoniae	*Proteus mirabilis*
ANAEROBIC SPECIES:	*Pseudomonas aeruginosa*
Propionibacterium acnes	*Serratia marcescens**

*Efficasy for this organism was studied in fewer than 10 infection

The safety and effectiveness of ofloxacin ophthalmic solution in treating ophthalmologic infections due to the following organisms have not been established in adequate and well-controlled clinical trials. Ofloxacin ophthalmic solution has been shown to be active *in vitro* against most strains of these organisms but the clinical significance in ophthalmologic infections is unknown.

AEROBES, GRAM-POSITIVE:	
Enterococcus faecalis	*Staphylococcus hominus*
Listeria monocytogenes	*Staphylococcus simulans*
Staphylococcus capitis	*Streptococcus pyogenes*
AEROBES, GRAM-NEGATIVE:	

Acinetobacter calcoaceticus var. anitratus	*Klebsiella pneumoniae*
Acinetobacter calcoaceticus var. lwoffii	*Moraxella (Branhamella) catarrhalis*
Citrobacter diversus	*Moraxella lacunata*
Citrobacter freundii	*Morganella morganii*
Enterobacter aerogenes	*Neisseria gonorrhoeae*
Enterobacter agglomerans	*Pseudomonas acidovorans*
Escherichia coli	*Pseudomonas fluorescens*
Haemophilus parainfluenzae	*Shigella sonnei*
Klebsiella oxytoca	
OTHER:	
Chlamydia trachomatis	

Clinical Studies:

Conjunctivitis: In a randomized, double-masked, multicenter clinical trial, ofloxacin ophthalmic solution was superior to its vehicle after 2 days of treatment in patients with conjunctivitis and positive conjunctival cultures. Clinical outcomes for the trial demonstrated a clinical improvement rate of 86% (54/63) for the ofloxacin treated group versus 72% (48/67) for the placebo treated group after 2 days of therapy. Microbiological outcomes for the same clinical trial demonstrated an eradication rate for causative pathogens of 65% (41/63) for the ofloxacin treated group versus 25% (17/67) for the vehicle treated group after 2 days of therapy. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

Corneal Ulcers: In a randomized, double-masked, multi-center clinical trial of 140 subjects with positive cultures, ofloxacin ophthalmic solution treated subjects had an overall clinical success rate (complete re-epithelialization and no progression of the infiltrate for two consecutive visits) of 82% (61/74) compared to 80% (53/66) for the fortified antibiotic group, consisting of 1.5% tobramycin and 10% cefazolin solutions. The median time to clinical success was 11 days for the ofloxacin treated group and 10 days for the fortified treatment group.

INDICATIONS AND USAGE

Ofloxacin ophthalmic solution is indicated for the treatment of infections caused by susceptible strains of the following bacteria in the conditions listed below:

CONJUNCTIVITIS:	
Gram-positive bacteria:	**Gram-negative bacteria:**
Staphylococcus aureus	*Enterobacter cloacae*
Staphylococcus epidermidis	*Haemophilus influenzae*
Streptococcus pneumoniae	*Proteus mirabilis*
	Pseudomonas aeruginosa
CORNEAL ULCERS:	
Gram-positive bacteria:	**Gram-negative bacteria:**
Staphylococcus aureus	*Pseudomonas aeruginosa*
Staphylococcus epidermidis	*Serratia marcescens**
Streptococcus pneumoniae	**Anaerobic species:**
	Propionibacterium acnes

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

CONTRAINDICATIONS

Ofloxacin Ophthalmic Solution is contraindicated in patients with a history of hypersensitivity to ofloxacin, to other quinolones, or to any of the components in this medication (see Warnings).

WARNINGS

NOT FOR INJECTION.

Ofloxacin ophthalmic solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

There are rare reports of anaphylactic reaction /shock and fatal hypersensitivity reactions in patients receiving systemic quinolones, some following the first dose, including ofloxacin. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including 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 ofloxacin. If an allergic reaction to ofloxacin occurs, discontinue the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management, including intubation should be administered as clinically indicated.

PRECAUTIONS

General:

As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs discontinue use and institute alternative therapy. Whenever clinical judgement dictates, the patient should be examined with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. Ofloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity reaction.

The systemic administration of quinolones, including ofloxacin, has led to lesions or erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species. Ofloxacin, administered systemically at 10 mg/kg/day in young dogs (equivalent to 110 times the maximum recommended daily adult ophthalmic dose) has been associated with these types of effects.

Information for Patients:

Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemic quinolones, including ofloxacin, have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions:

Specific drug interaction studies have not been conducted with ofloxacin ophthalmic solution. However, the systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, and enhance the effects of the oral anticoagulant warfarin and its derivatives, and has been associated with transient elevations in serum creatinine in patients receiving cyclosporine concomitantly.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long term studies to determine the carcinogenic potential of ofloxacin have not been conducted.

Ofloxacin was not mutagenic in the Ames test, *in vitro* and *in vivo* cytogenic assay, sister chromatid exchange assay (Chinese hamster and human cell lines), unscheduled DNA synthesis (UDS) assay using human fibroblasts, the dominant lethal assay, or mouse micronucleus assay. Ofloxacin was positive in the UDS test using rat hepatocyte, and in the mouse lymphoma assay.

In fertility studies in rats, ofloxacin did not affect male or female fertility or morphological or reproductive performance at oral dosing up to 360 mg/kg/day (equivalent to 4000 times the maximum recommended daily ophthalmic dose).

Pregnancy:

Teratogenic Effects:

Ofloxacin has been shown to have an embryocidal effect in rats and in rabbits when given in doses of 810 mg/kg/day (equivalent to 9000 times the maximum recommended daily ophthalmic dose) and 160 mg/kg/day (equivalent to 1800 times the maximum recommended daily ophthalmic dose). These dosages resulted in decreased fetal body weight and increased fetal mortality in rats and rabbits, respectively. Minor fetal skeletal variations were reported in rats receiving doses of 810 mg/kg/day. Ofloxacin has not been shown to be teratogenic at doses as high as 810 mg/kg/day and 160 mg/kg/day when administered to pregnant rats and rabbits, respectively.

Nonteratogenic Effects:

Additional studies in rats with doses up to 360 mg/kg/day during late gestation showed no adverse effect on late fetal development, labor, delivery, lactation, neonatal viability, or growth of the newborn.

There are, however, no adequate and well-controlled studies in pregnant women. Ofloxacin ophthalmic solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

In nursing women a single 200 mg oral dose resulted in concentrations of ofloxacin in milk which were similar to those found in plasma. It is not known whether ofloxacin is excreted in human milk following topical ophthalmic administration. Because of the potential for serious adverse reactions from ofloxacin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

Safety and effectiveness in infants below the age of one year have not been established.

Quinolones, including ofloxacin, have been shown to cause arthropathy in immature animals after oral administration; however, topical ocular administration of ofloxacin to immature animals has not shown any arthropathy. There is no evidence that the ophthalmic dosage form of ofloxacin has any effect on weight bearing joints.

Geriatric Use:

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Ophthalmic Use: The most frequently reported drug-related adverse reaction was transient ocular burning or discomfort. Other reported reactions include stinging, redness, itching, chemical conjunctivitis/keratitis, ocular/periocular/facial edema, foreign body sensation, photophobia, blurred vision, tearing, dryness, and eye pain. Rare reports of dizziness and nausea have been received. Refer to Warnings for additional adverse reactions.

To report SUSPECTED ADVERSE REACTIONS, contact Rising Pharma Holdings, Inc. at 1-844-874-7464 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

The recommended dosage regimen for the treatment of **bacterial conjunctivitis** is:

Days 1 and 2	Instill one to two drops every two to four hours in the affected eye(s).
Days 3 through 7	Instill one to two drops four times daily.
The recommended dosage regimen for the treatment of **bacterial corneal ulcer** is:	
Days 1 and 2	Instill one to two drops into the affected eye every 30 minutes, while awake. Awaken at approximately four and six hours after retiring and instill one to two drops.
Days 3 through 7 to 9	Instill one to two drops hourly, while awake.
Days 7 to 9 throughtreatment completion	Instill one to two drops, four times daily.

HOW SUPPLIED

Ofloxacin Ophthalmic Solution 0.3% is supplied sterile in a labeled translucent LDPE bottle with insert cap assembly comprising of tan colored HDPE screw cap over a LDPE nozzle with tamper-evident LDPE dust cover sealing the bottle cap.

5 mL in 5 mL bottle NDC 64980-515-05

10 mL in 10 mL bottle NDC 64980-515-01

Note: Store at 20° to 25°C (68° to 77°F)[see USP Controlled Room Temperature].

Rx Only

Manufactured By:

FDC Limited,

B-8, MIDC Industrial Area,

Waluj, Aurangabad - 431 136,

Maharashtra, India

Toll free number: 1-800-521-5340

Distributed by:

Rising Pharma Holdings, Inc.

East Brunswick, NJ 08816

Revised: 06/2024

INSTRUCTIONS FOR USE

Please follow these instructions carefully when using Ofloxacin Ophthalmic Solution.

Use Ofloxacin ophthalmic solution as prescribed by your doctor.

1. If you use other topically applied ophthalmic medications, they should be administered at least 10 minutes before or after the use of Ofloxacin ophthalmic solution.

2. Wash hands before each use.

3. Before using the medication for the first time, be sure the dust cover seal is unbroken.

4. Refer (I-VI)

Bottle as you receive it

Image

Snap off the dust cover by turning it clockwise to break the seal

Image

Pull off the dust cover

Image

Unscrew the tan coloured cap

Image

Tilt your head backward and pull your lower eyelid down slightly to form pocket between your eyelid and your eye. Dispense drops with gentle pressure.

Image

Replace the tan coloured cap after every use, and screw the cap down

Image

5. OPHTHALMIC MEDICATIONS, IF HANDLED IMPROPERLY, CAN BECOME CONTAMINATED BY COMMON BACTERIA KNOWN TO CAUSE EYE INFECTIONS. SERIOUS DAMAGE TO THE EYE AND SUBSEQUENT LOSS OF VISION MAY RESULT FROM USING CONTAMINATED OPHTHALMIC MEDICATIONS. IF YOU THINK YOUR MEDICATION MAY BE CONTAMINATED, OR IF YOU DEVELOP AN EYE INFECTION, CONTACT YOUR DOCTOR IMMEDIATELY CONCERNING CONTINUED USE OF THIS BOTTLE.

6. Repeat (V) and (VI) with the other eye if instructed to do by your doctor.

7. The insert tip is designed to provide a premeasured drop; therefore, do NOT enlarge the hole of the insert tip.

8. After you have used all doses, there will be some Ofloxacin Ophthalmic Solution left in the bottle. You should not be concerned since an extra amount of Ofloxacin Ophthalmic Solution has been added and you will get the full amount of Ofloxacin Ophthalmic Solution that your doctor prescribed. Do not attempt to remove excess medicine from the bottle.

WARNING: KEEP OUT OF REACH OF CHILDREN.

IF YOU HAVE ANY QUESTIONS ABOUT THE USE OF OFLOXACIN OPHTHALMIC SOLUTION, PLEASE CONSULT YOUR DOCTOR.

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Ofloxacin Ophthalmic Solution 0.3% 5 mL Container

Rising Pharma Holdings, Inc. **NDC 64980-515-05**

Ofloxacin Ophthalmic Solution USP

Rx Only **0.3%** **5 mL**

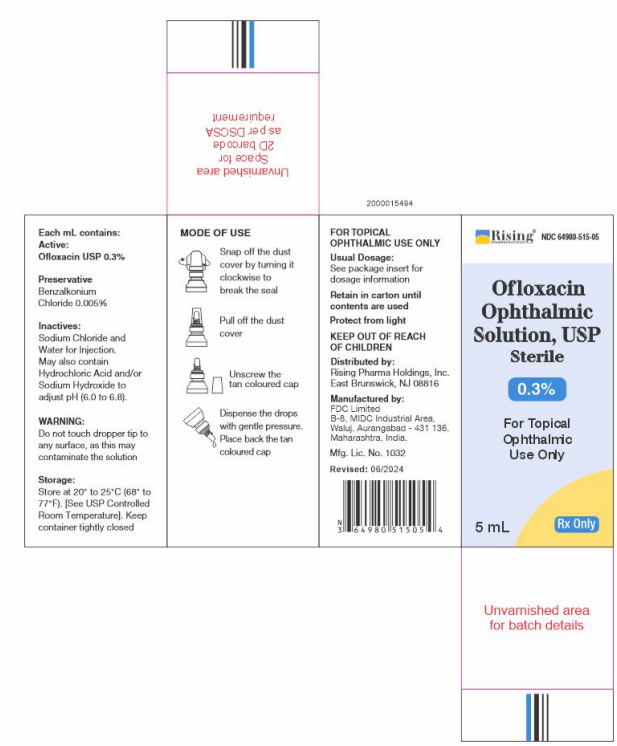
Active: Ofloxacin USP 0.3%

Preservative: Benzalkonium Chloride (0.005%)

Usual Dosage: See package insert.

FOR TOPICAL OPHTHALMIC USE ONLY

Retain in carton until contents are used. Protect from light.



Ofloxacin Ophthalmic Solution 0.3% 10 mL Container

Rising Pharma Holdings, Inc. **NDC 64980-515-01**

Ofloxacin Ophthalmic Solution USP

Rx Only **0.3%** **10 mL**

Active: Ofloxacin USP 0.3%

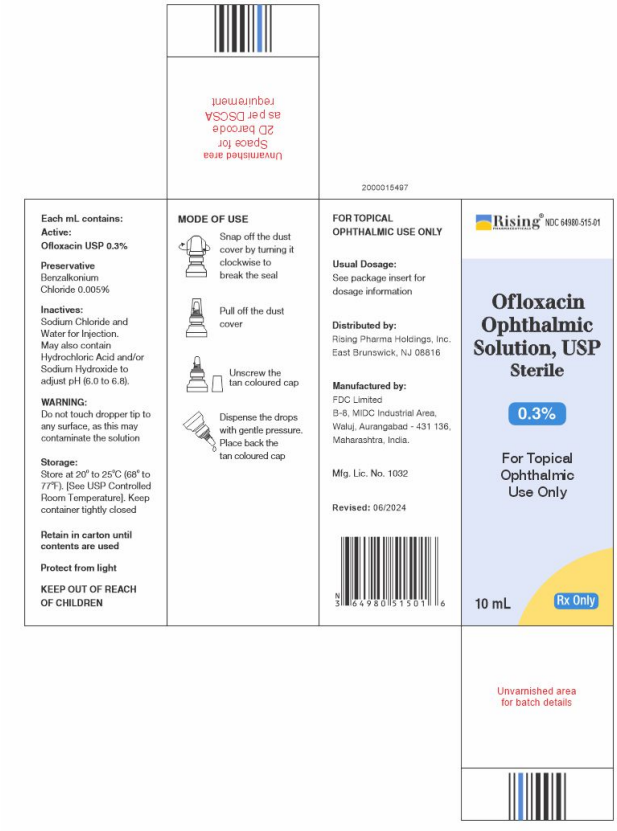
Preservative: Benzalkonium Chloride (0.005%)

Usual Dosage: See package insert.

FOR TOPICAL OPHTHALMIC USE ONLY

Retain in carton until contents are used.

Protect from light.



OFLOXACIN

ofloxacin solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64980-515
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
OFLOXACIN (UNII: A4P49JAZ9H) (OFLOXACIN - UNII:A4P49JAZ9H)	OFLOXACIN	3 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)	0.05 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64980-515-01	1 in 1 CARTON	11/01/2017	
1		10 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		
2	NDC:64980-515-05	1 in 1 CARTON	11/01/2017	
2		5 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA078559	12/15/2014	

Labeler - Rising Pharma Holdings, Inc. (116880195)

Registrant - FDC Limited (650078413)

Establishment

Name	Address	ID/FEI	Business Operations
FDC Limited		862267994	ANALYSIS(64980-515) , MANUFACTURE(64980-515)

Revised: 8/2024 Rising Pharma Holdings, Inc.