OFLOXACIN- ofloxacin solution/ drops
NuCare Pharmaceuticals,Inc.

Ofloxacin Ophthalmic

Solution 0.3%

Sterile

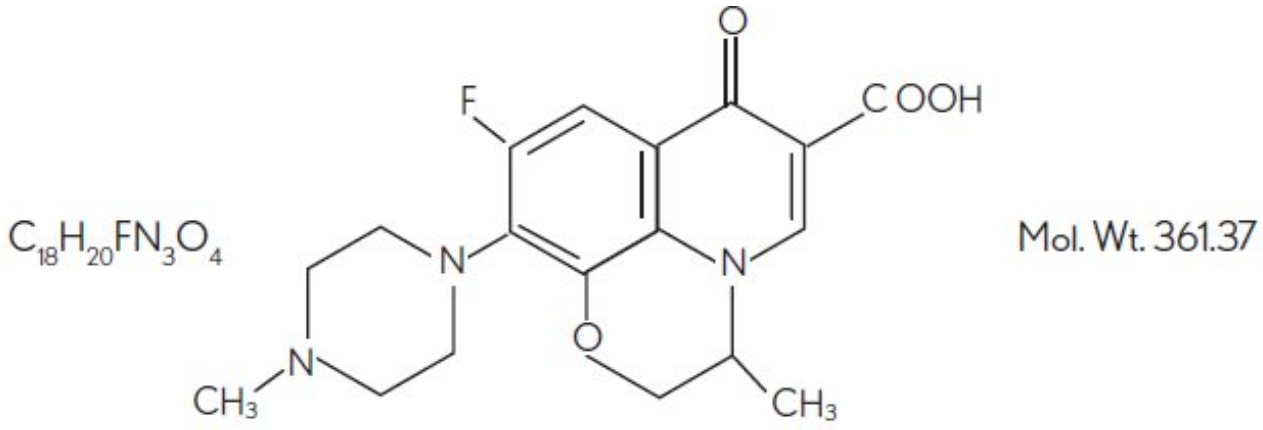
Rx only

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.



CONTAINS: ACTIVE: ofloxacin 0.3% (3 mg/mL)
PRESERVATIVE ADDED: benzalkonium chloride (0.005%)
INACTIVES: sodium chloride and purified water. May also contain hydrochloric acid and/or sodium hydroxide may be added 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:
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae

AEROBES, GRAM-NEGATIVE:
Enterobacter cloacae
Haemophilus influenzae
Proteus mirablis
Pseudomonas aeruginosa
*Serratia marcescens**

ANAEROBIC SPECIES:
Propionibacterium acnes

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

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
Listeria monocytogenes
Staphylococcus capitis
Staphylococcus hominus
Staphylococcus simulans
Streptococcus pyogenes

AEROBES, GRAM-NEGATIVE:
Acinetobacter calcoaceticus var. anitratus
Acinetobacter calcoaceticus var. lwoffi
Citrobacter diversus
Citrobacter freundii
Enterobacter aerogenes
Enterobacter agglomerans
Escherichia coli
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Moraxella (Branhamella) catarrhalis
Moraxella lacunata
Morganella morganii
Neisseria gonorrhoeae
Pseudomonas acidovorans
Pseudomonas fluorescens
Shigella sonnei

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, multicenter 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:

Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae

Gram-negative bacteria:
Enterobacter cloacae
Haemophilus influenzae
Proteus mirabilis
Pseudomonas aeruginosa

CORNEAL ULCERS:

Gram-positive bacteria:
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae

Gram-negative bacteria:
Pseudomonas aeruginosa
*Serratia marcescens**

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 judgment 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 Bausch & Lomb Incorporated at 1-800-321-4576 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:

1. 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:

1. 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.
2. Days 7 to 9 through Instill one to two drops, four times daily.
   treatment completion

DO NOT USE IF IMPRINTED "Protective Seal" WITH YELLOW IS NOT INTACT.

HOW SUPPLIED

Ofloxacin Ophthalmic Solution 0.3% is supplied sterile in plastic dropper bottles with tan caps in the following sizes:

5 mL NDC 68071-2254-5

NOTE: Store at 15° to 25°C (59° to 77°F).

KEEP OUT OF REACH OF CHILDREN.

FOR OPHTHALMIC USE ONLY.

Distributed by:
Bausch & Lomb, a division of Bausch Health US, LLC, Bridgewater, NJ 08807 USA

Manufactured by:
Bausch & Lomb Incorporated
Tampa, FL 33637 USA

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9118304 (**FOLDED**)
9118204 (**FLAT**)

Rev. 06/2019

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL



OFLOXACIN

ofloxacin solution/ drops

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68071-2254(NDC:24208-434)
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)	
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:68071-2254-5	1 in 1 CARTON	09/03/2020	

1		5 mL in 1 BOTTLE, DROPPER; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076622	05/14/2004	

Labeler - NuCare Pharmaceuticals,Inc. (010632300)

Establishment

Name	Address	ID/FEI	Business Operations
NuCare Pharmaceuticals,Inc.		010632300	relabel(68071-2254)

Revised: 1/2022 NuCare Pharmaceuticals,Inc.