OFLOXACIN (Ophthalmic)

Introduction

Category

Antibacterial (ophthalmic).

Indications

Accepted

Conjunctivitis, bacterial (treatment)¾Ophthalmic ofloxacin is indicated in the treatment of conjunctivitis caused by susceptible strains of Enterobacter cloacae , Haemophilus influenzae , Proteus mirabilis , Pseudomonas aeruginosa , Staphylococcus aureus , Staphylococcus epidermidis , and Streptococcus pneumoniae. 1, 3, 4, 5, 7, 8

Not all species or strains of a particular organism may be susceptible to ofloxacin.

Corneal ulcers, bacterial (treatment) 8, *¾Ophthalmic ofloxacin is indicated in the treatment of corneal ulcers caused by susceptible strains of Propionibacterium acnes , P. aeruginosa , Serratia marcescens , S. aureus , S. epidermidis , and S. pneumoniae. 8

Efficacy for S. marcescens was studied in less than ten infections. 8

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to fluoroquinolones or their derivatives, such as cinoxacin, ciprofloxacin, enoxacin, lomefloxacin, nalidixic acid, or norfloxacin, may be sensitive to ofloxacin also. 1

Carcinogenicity

Studies to determine the carcinogenic potential of ofloxacin have not been done. 1

Mutagenicity

Ofloxacin was mutagenic in the unscheduled DNA synthesis (UDS) test using rat hepatocytes and in the mouse lymphoma assay. However, ofloxacin was not mutagenic in the UDS assay using human fibroblasts, the Ames test, in vitro and in vivo cytogenic assay, sister chromatid exchange assay (Chinese hamster and human cell lines), dominant lethal assay, or mouse micronucleus assay. 1

Pregnancy/Reproduction

Fertility¾In studies in rats, ofloxacin did not affect male or female fertility when given orally in doses of up to 360 mg per kg of body weight (mg/kg) per day. 1

Pregnancy¾Adequate and well-controlled studies have not been done in humans. 1

Studies using ophthalmic ofloxacin have not been done in animals. However, systemic doses below 810 mg/kg per day in rats and below 160 mg/kg per day in rabbits were not shown to be teratogenic. Doses of 810 mg/kg per day in rats resulted in decreased fetal body weight and minor fetal skeletal variations; rabbits given doses of 160 mg/kg per day showed an increase in fetal mortality. 1

In addition, although systemic ofloxacin has been shown to cause arthropathy in immature animals, ophthalmic ofloxacin has not caused arthropathy or had any other effect on weight-bearing joints in immature animals. 1

FDA Pregnancy Category C. 1

Labor¾Studies in rats given systemic doses of ofloxacin of up to 360 mg/kg per day during late gestation showed no adverse effect of the medication on labor. 1

Delivery¾Studies in rats given systemic doses of ofloxacin of up to 360 mg/kg per day during late gestation showed no adverse effect of the medication on delivery. 1

Breast-feeding

It is not known whether ophthalmic ofloxacin is distributed into breast milk. An orally administered dose of 200 mg of ofloxacin in nursing women resulted in concentrations of ofloxacin in the milk that were similar to its concentrations in plasma. However, for ophthalmic ofloxacin, the dose is much smaller and the plasma concentration is much lower than those of oral ofloxacin. 1

Pediatrics

Appropriate studies on the relationship of age to the effects of ophthalmic ofloxacin have not been performed in children up to 1 year of age. Safety and efficacy have not been established. 1

Although ofloxacin and other quinolones cause arthropathy in immature animals after oral administration, ophthalmic ofloxacin administered to immature animals did not cause arthropathy. In addition, there is no evidence that the ophthalmic dosage form has any effect on the weight-bearing joints. 1

Geriatrics

Appropriate studies on the relationship of age to the effects of ophthalmic ofloxacin have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.

Drug interactions and/or related problems

Drug interaction studies have not been performed with the ophthalmic dosage form of ofloxacin. 8 However, it is known that systemic ofloxacin may elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, and enhance the clinical effects of warfarin. 8 Systemic

ofloxacin has also been associated with a transient elevation of serum creatinine in patients who received cyclosporine. 8

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problem exists

>> Sensitivity to ofloxacin or other fluoroquinolones or their derivatives 1

Side/Adverse Effects

Note: An incident of Stevens-Johnson syndrome that progressed to toxic epidermal necrolysis was reported in a patient who was receiving topical ophthalmic ofloxacin. 8 Systemic quinolones, including ofloxacin, have been associated with serious and occasionally fatal hypersensitivity reactions, some of which involved cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal, or facial edema), airway obstruction, dyspnea, urticaria, and itching. 8 Prolonged use of anti-infectives, including ofloxacin, may result in the overgrowth of nonsusceptible organisms, including fungi. 8

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence rare

Dizziness 1; hypersensitivity reactions (itching, rash, or hives; swelling of face or lips; tightness in chest or wheezing; troubled breathing); periocular or facial edema (swelling or puffiness of eye or face)
Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Burning of eye 1
Incidence less frequent

Blurred vision; chemical conjunctivitis or keratitis (redness, irritation, or itching of eye, eyelid, or inner lining of eyelid); eye pain; foreign body sensation (feeling of something in the eye); photophobia 1 (increased sensitivity of eye to light); stinging, redness, itching, tearing, or dryness of eye 1, 6

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Ofloxacin (Ophthalmic) .
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to ofloxacin or other fluoroquinolones or their derivatives
Pregnancy¾Studies using ophthalmic ofloxacin have not been done; however, studies in animals given very high doses of systemic ofloxacin have shown fetotoxicity
Breast-feeding¾Oral ofloxacin is distributed into breast milk; it is not known whether ophthalmic ofloxacin is distributed into breast milk
Use in children¾Safety and efficacy have not been established in infants up to 1 year of age
Proper use of this medication

Proper administration technique

>> Compliance with full course of therapy

>> Proper dosing
Missed dose: Applying as soon as possible; not applying if almost time for next dose
>> Proper storage
Precautions while using this medication

Checking with physician if no improvement within 7 days

>> Discontinuing use of ofloxacin and contacting physician if rash or allergic reaction occurs

Possible photophobic reactions; wearing sunglasses and avoiding prolonged exposure to bright light

Side/adverse effects

Signs of potential side effects, especially dizziness, hypersensitivity reactions, and periocular or facial edema

General Dosing Information

Ofloxacin ophthalmic solution is not for injection into the eye. 1

Although some manufacturers recommend doses of 2 drops of ophthalmic solutions at appropriate intervals, the conjunctival sac usually holds less than 1 drop.
If hypersensitivity develops, therapy with ophthalmic ofloxacin should be discontinued. 1

For treatment of adverse effects

Recommended treatment consists of the following:
· For mild hypersensitivity reaction¾Administering antihistamines and, if necessary, glucocorticoids.
· For severe hypersensitivity or anaphylactic reaction¾Administering epinephrine. Oxygen and airway management, including intubation, should be administered if clinically appropriate. 8 Antihistamines and/or glucocorticoids may also be administered as required.

· For superinfection¾Ophthalmic ofloxacin should be discontinued and an alternative therapy started. 8 If clinically appropriate, the eye should be examined with the aid of magnification, such as slit lamp biomicroscopy, and, if appropriate, fluorescein staining. 8

Ophthalmic Dosage Forms

OFLOXACIN OPHTHALMIC SOLUTION

Usual adult and adolescent dose

Bacterial conjunctivitis¾
Topical, to the conjunctiva, 1 drop in affected eye every two to four hours, while patient is awake, for two days; then, 1 drop four times a day for up to five more days. 1, 8

Bacterial corneal ulcers 8¾
Topical, to the conjunctiva, 1 drop in affected eye every thirty minutes, while patient is awake, and 1 drop four to six hours after retiring, for two days; then, 1 drop every hour while awake for up to seven more days; then, 1 drop four times a day from the seventh, eighth, or ninth day through treatment completion. 8

Usual pediatric dose

Bacterial conjunctivitis¾
Infants up to 1 year of age: Safety and efficacy have not been established. 1

Children 1 year of age and older: See Usual adult and adolescent dose.

Bacterial corneal ulcers¾
Infants up to 1 year of age: Safety and efficacy have not been established. 1

Children 1 year of age and older: See Usual adult and adolescent dose.

Strength(s) usually available

U.S.¾0.3% (Rx)[Ocuflox 1, 8 (benzalkonium chloride 0.005%) (sodium chloride) (hydrochloric acid) (sodium hydroxide)]

Canada¾0.3% (Rx)[Ocuflox 9 (benzalkonium chloride 0.005%) (sodium chloride) (hydrochloric acid) (sodium hydroxide)]

Packaging and storage:

Store between 15 and 25 °C (59 and 77 °F), unless otherwise specified by manufacturer. 1

Auxiliary labeling:

· For the eye. 1

References

1 Ocuflox package insert (Allergan¾US), Rev 7/93, Rec 10/93.

2 Fleeger CA, editor. USAN 1993. USAN and the USP dictionary of drug names. Rockville, MD: The United States Pharmacopeial Convention, Inc., 1992: 458.

3 Osato MS, Jensen HG, Trousdale MD, et al. The comparative in vitro activity of ofloxacin and selected ophthalmic antimicrobial agents against ocular bacterial isolates [published erratum appears in Am J Ophthalmol 1991 Oct 15; 112(4): 478-9]. Am J Ophthalmol 1989 Oct 15; 108(4): 380-6.

4 Gwon A. Topical ofloxacin compared with gentamicin in the treatment of external ocular infection. Ofloxacin Study Group. Br J Ophthalmol 1992 Dec; 76(12): 714-8.

5 Gwon A. Ofloxacin vs tobramycin for the treatment of external ocular infection. Ofloxacin Study Group II. Arch Ophthalmol 1992 Sep; 110(9): 1234-7.

6 Borrmann L, Tang-Liu DD, Kann J, et al. Ofloxacin in human serum, urine, and tear film after topical application. Cornea 1992 May; 11(3): 226-30.

7 Bron AJ, Leber G, Rizk SN, et al. Ofloxacin compared with chloramphenicol in the management of external ocular infection. Br J Ophthalmol 1991 Nov; 75(11): 675-9.

8 Ocuflox package insert
9 Ocuflox (Allergan). In: Gillis MC, editor. CPS Compendium of pharmaceuticals and specialties. 33rd ed. Ottawa: Canadian Pharmacists Association; 1998. p. 1202-3.