

Leeflox

Levofloxacin 0.5% Eye Drops

DESCRIPTION:

LEEFLOX (levofloxacin ophthalmic solution) 0.5% is a sterile topical ophthalmic solution. Levofloxacin is a fluoroquinolone antibacterial active against a broad spectrum of Gram-positive and Gram-negative ocular pathogens. Levofloxacin is the pure (-)-(S)-enantiomer of the racemic drug substance, ofloxacin. It is more soluble in water at neutral pH than ofloxacin.

Each mL of LEEFLOX contains 5.12 mg of levofloxacin hemihydrate equivalent to 5 mg levofloxacin.



CLINICAL PHARMACOLOGY:

Pharmacokinetics:

The mean levofloxacin concentration in plasma 1 hour post-dose, ranged from 0.86 ng/mL on Day 1 to 2.05 ng/mL on Day 15.

The highest maximum mean levofloxacin concentration of 2.5 ng/mL was measured on Day 4 following 2 days of dosing every 2 hours for a total of 8 doses per day.

Maximum mean levofloxacin concentrations increased from 0.94 ng/mL on Day 1 to 2.15 ng/mL on Day 15, which is more than 1,000 times lower than those reported after standard oral doses of levofloxacin.

Levofloxacin concentration in tears was measured in 30 healthy adult volunteers at various time points following instillation of a single drop of **LEEFLOX** solution. Mean levofloxacin concentrations in tears ranged from 34.9 to 221.1 mcg/mL during the 60-minute period following the single dose. The mean tear concentrations measured 4 and 6 hours postdose were 17.0 and 6.6 mcg/mL.

Microbiology:

The mechanism of action of levofloxacin and other fluoroquinolone antimicrobials involves the inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair, and recombination. Levofloxacin has in vitro activity against a wide range of Gram-negative and Gram-positive microorganisms and is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations.

Levofloxacin exhibits in vitro minimal inhibitory concentrations (MICs) of 2mcg/mL or less (systemic susceptible breakpoint) against most (•90%) strains of the following ocular pathogens:

Aerobic gram-positive microorganisms

Staphylococcus aureus
Staphylococcus saprophyticus

Streptococcus pneumoniae
Streptococcus pyogenes

Aerobic gram-negative microorganisms

Moraxella catarrhalis
Neisseria gonorrhoeae
Proteus vulgaris
Escherichia coli
Pseudomonas aeruginosa
Klebsiella pneumoniae

Haemophilus parainfluenzae
Proteus mirabilis
Providencia rettgeri
Citrobacter freundii
Pseudomonas fluorescens

INDICATIONS AND USAGE

Bacterial Conjunctivitis due to susceptible organisms.

CONTRAINDICATIONS

LEEFLOX solution is contraindicated in patients with a history of hypersensitivity to Levofloxacin, to other quinolones, or to any of the components of this medication.

WARNINGS

NOT FOR INJECTION.

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

PRECAUTIONS

General

As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible 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. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients

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

Drug Interactions:

Specific drug interaction studies have not been conducted with **LEEFLOX**. 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 systemic cyclosporine concomitantly.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

In a long-term carcinogenicity study in rats, levofloxacin exhibited no carcinogenic or tumorigenic potential following daily dietary administration; the highest dose (100 mg/kg/day) was 875 times the highest recommended human ophthalmic dose.

Levofloxacin was not mutagenic in the following assays:

Ames bacterial mutation assay (*S. typhimurium* and *E. coli*), CHO/HGPRT forward mutation assay, mouse micronucleus test, mouse dominant lethal test, rat unscheduled DNA synthesis assay, and the in vivo mouse sister chromatid exchange assay. It was positive in the in vitro chromosomal aberration (CHL cell line) and in vitro sister chromatid exchange (CHL/IU cell line) assays.

Levofloxacin caused no impairment of fertility or reproduction in rats at oral doses as high as 360 mg/kg/day, corresponding to 3,150 times the highest recommended human ophthalmic dose.

Pregnancy (Teratogenic Effects):

Levofloxacin at oral doses of 810 mg/kg/day in rats, which corresponds to approximately 7,000 times the highest recommended human ophthalmic dose, caused decreased fetal body weight and increased fetal mortality.

No teratogenic effect was observed when rabbits were dosed orally as high as 50 mg/kg/day, which corresponds to approximately 400 times the highest recommended maximum human ophthalmic dose, or when dosed intravenously as high as 25 mg/kg/day, corresponding to approximately 200 times the highest recommended human ophthalmic dose. There are, however, no adequate and well-controlled studies in pregnant woman. Levofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

Levofloxacin has not been measured in human milk. Based upon data from ofloxacin, it can be presumed that levofloxacin is excreted in human milk. Caution should be exercised when **LEEFLOX** is administered to a nursing mother.

Pediatric Use:

Safety and effectiveness in infants below the age of one year have not been established. Oral administration of quinolones has been shown to cause arthropathy in immature animals. There is no evidence that the ophthalmic administration of levofloxacin has any effect on weight bearing joints.

Geriatric Use:

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

ADVERSE REACTIONS

The most frequently reported adverse events in the overall study populations were transient decreased vision, fever, foreign body sensation, headache, transient ocular burning, ocular pain or discomfort, pharyngitis and photophobia. These events occurred in approximately 1-3% of patients.

Other reported reactions occurring in less than 1% of patients included allergic reactions, lid edema, ocular dryness and ocular itching.

DOSAGE AND ADMINISTRATION

Days 1 and 2:

Instill one to two drops in the affected eye(s) every 2 hours while awake, up to 8 times per day.

Days 3 through 7:

Instill one to two drops in the affected eye(s) every 4 hours while awake, up to 4 times per day.

HOW SUPPLIED

LEEFLOX (levofloxacin ophthalmic solution) 0.5% is supplied in a transparent plastic bottle of 5 mL.

Storage:

Store at 15⁰ -25⁰ C