VOLOXAL 0.5 %

Eye Drops

Composition
Levofloxacin 0.5% (5 mg/mL)

Action
Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antimicrobial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. 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.

Fluoroquinolones, including levofloxacin, differ in chemical structure and mode of action from β-lactam antibiotics and aminoglycosides, and therefore may be active against bacteria resistant to β-lactam antibiotics and aminoglycosides. Additionally, β-lactam antibiotics and aminoglycosides may be active against bacteria resistant to levofloxacin.
Resistance to levofloxacin due to spontaneous mutation in vitro is a rare occurrence (range: 10-9 to 10-10).

Levofloxacin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections:

Aerobic gram-positive microorganisms
*Corynebacterium species **
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus (Groups C/F)
Streptococcus (Group G)
Viridans group streptococci

Aerobic gram-negative microorganisms
*Acinetobacter lwoffii **
Haemophilus influenzae
*Serratia marcescens **

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

The following in vitro data are also available, but their clinical significance in ophthalmic infections is unknown. The safety and effectiveness of levofloxacin in treating ophthalmological infections due to these microorganisms have not been established in adequate and well-controlled trials .

These organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the in vitro systemic breakpoint and ophthalmological efficacy has not been established. The list of organisms is provided as guidance only in assessing the potential treatment of conjunctival infections. Levofloxacin exhibits in vitro minimal inhibitory concentrations (MICs) of 2 µg/mL or less (systemic susceptible breakpoint) against most (≥90%) strains of the following ocular pathogens.

Aerobic gram-positive microorganisms
Enterococcus faecalis
Staphylococcus saprophyticus

Streptococcus agalactiae
Streptococcus pyogenes

Aerobic gram-negative microorganisms
Acinetobacter anitratus
Acinetobacter baumannii
Citrobacter diversus
Citrobacter freundii
Enterobacter aerogenes
Enterobacter agglomerans
Enterobacter cloacae
Escherichia coli
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Legionella pneumophila
Moraxella catarrhalis
Morganella morganii
Neisseria gonorrhoeae
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Pseudomonas aeruginosa
Pseudomonas fluorescens

Pharmacokinetics

Levofloxacin concentration in plasma was measured in 15 healthy adult volunteers at various time points during a 15-day course of treatment with Levofloxacin 0.5% solution. 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 2.25 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 Levofloxacin 0.5% solution. Mean levofloxacin concentrations in tears ranged from 34.9 to 221.1 µg/mL during the 60-minute period following the single dose. The mean tear concentrations measured 4 and 6 hours post dose were 17.0 and 6.6 µg/mL. The clinical significance of these concentrations is unknown.

Indications

Voloxal 0.5% solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic gram-positive microorganisms
*Corynebacterium species**
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus (Groups C/F)
Streptococcus (Group G)
Viridans group streptococci

Aerobic gram-negative microorganisms
*Acinetobacter Iwoffii**

Haemophilus influenzae
*Serratia marcescens**

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

Contraindications
Contraindicated in patients with a history of hypersensitivity to levofloxacin, to other quinolones, or to any of the components in this medication.

Warnings
Not for injection
Voloxal solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemic quinolones, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to levofloxacin occurs, discontinue the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Adverse Reactions
The most frequently reported adverse events in the overall study population 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.

Precautions
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.

Pregnancy
Category C
Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

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 Levofloxacin 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.

Drug Interactions

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

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.

Presentation

Dropper bottle of 5 ml