ULTRACIN

Eye & Ear Drops

Composition
Each ml contains Ofloxacin 3 mg.

Action
Ofloxacin has in vitro activity against abroad 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 thought to exert a bactericidal effect on susceptible bacterial cells by inhibiting DNA gyrase, an essential bacterial enzyme that 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.

Ultracin 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.

Aerobes, gram-positive
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneumoniae

Aerobes, gram-negative
Enterobacter cloacae
Haemophilus influenza
Proteus mirabilis
Pseudomonas aeruginosa
*Serratia marcescens**

Anaerobic species
Propionibacterium acnes

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

The safety and effectiveness of Ultracin in treating ophthalmologic infections due to the following organisms have not been established in adequate and well-controlled clinical trials, Ultracin 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. Iwoffii
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 sonnet

Other
Chlamydia trachomatis

Ofloxacin has been shown to be active against most strains of the following organisms both in vitro and clinically in otic infections:
Aerobes, gram-positive
Staphylococcus aureus
Streptococcus pneumonia

Aerobes, gram-negative
Haemophilus influenza
Moraxella catarrhalis
Proteus mirabilis
Pseudomonas aeruginosa

Pharmacokinetics (Ocular administration)
Systemic absorption of ofloxacin was detected following ocular drug administration. The systemic absorption of ofloxacin was in the low ng/ml range.
The maximal serum concentration observed after topical ocular doses to man (± 1,9 ng/ml) was about a thousand fold lower than that achieved after a standard dose. Therefore, the pharmacokinetic parameters of ofloxacin following oral administration of therapeutic systemic dosages may not be clinically relevant to topical ocular administration due to the extremely low serum levels following topical administration.

Indications

Ultracin for Ophthalmic use
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 pneomoniae
Gram-negative bacteria
Enterobacter cloacae
Haemophilus influenzae
Proteus mirabilis
Pseudomonas aeruginosa

Anaerobic species
Propionibacterium acnes

Corneal Ulcers

Gram-positive bacteria
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus pneomoniae
Gram-negative bacteria
Pseudomonas aeroginsa
*Serratia marcescens**

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

Ultracin for Otic use
Indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below:
Otitis Externa
In adults and pediatric patients, one year and older, due to Staphylococcus aureus and Pseudomonas aeruginosa.

Chronic Suppurative Otitis Media
In patients 12 years and older with perforated tympanic membranes due to Staphylococcus aureus, Proteus mirabilis, and Pseudomonas aeruginosa.

Acute Otitis Media
In pediatric patients one year and older with tympanostomy tubes due to Staphylococcus aureus. Streptococcus pneumoniae, Haemophilus influenza, Moraxella catarrhalis, and Pseudomonas aeruginosa.

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

Warnings
Not for injection
Ofloxacin solution should not be injected subconjunctivally, or introduced directly into the anterior chamber of the eye.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions: some following the first dose have been reported in patients receiving systemic quinolones, 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 in- tubation should be administered as clinically indicated.

In case of eardrops, if an allergic reaction to Ofloxacin suspected, stop the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management, including in-tubation, should be administered as clinically indicated.

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, periocular/facial edema, foreign body sensation, photophobia, blurred vision, tearing, dryness, and eye pain, rare reports of dizziness have been received.

Otic use
Subjects with Otitis Externa
The following treatment-related adverse events occurred in 1% or more of the subjects with intact tympanic membranes.
Pruritus, Dizziness, Earache, Vertigo

Subjects with Acute Otitis Media with tympanostomy Tubes and Subjects with Chronic Suppurative Otitis Media with Perforated Tympanic Membranes
The following treatment-related adverse events occurred in 1% or more of the subjects with non-intact tympanic membranes.

Pruritus, Dizziness, Earache, Taste Perversion, Paraesthesia, and Rash

Precautions

For Ophthalmic use

General

As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If super infection 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 sigh 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 sign 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 effect

For Otic use

General

As with other anti-infective preparations, prolonged use may result in over-growth of non-susceptible organisms, including fungi. If the infection doses not improve after one week, cultures should be obtained to guide further treatment. If otorrhea persists after a full course of therapy, or if two or more episodes of otorrhea occur within six months, further evaluation is recommended to exclude an underlying condition such as cholesteatoma, foreign body, or a tumor.

The systemic administration of quinolones, including Ofloxacin at doses much higher than given or absorbed by the otic route, has led to lesions or erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species.

In case of Otitis Externa

Prior to administration of Ofloxacin Otic in patients with otitis externa, the solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness that may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops instilled. This position should be maintained for five minutes to facilitate penetration of the drops into the ear canal. Repeat, if necessary.

In case Acute Otitis Media and Chronic Suppurative Otitis Media

In pediatric patients (from 1 to 12 years old) with acute otitis media with tympanostomy tubes and in patients with chronic suppurative otitis media with perforated tympanic membranes, prior to administration, the solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be instilled. The tragus should then be pumped 4 times by pushing inward to facilitate penetration of the drops into the middle ear. This position should be maintained for five minutes. Repeat, if necessary.

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

In nursing women, a single 200 mg oral dose resulted in concentrations of Ofloxacin in milk that were similar to those found in plasma. It is unknown whether Ofloxacin excretes in human milk following topical ophthalmic and otic 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
For Ophthalmic use
Safety and effectiveness in infants below the age of one year have not been established. There is no evidence that the ophthalmic dosage form of Ofloxacin has any effect on weight bearing joints.

For Otic use
No changes in hearing function occurred in 30 pediatric subjects treated with Ofloxacin Otic and tested for audiometric parameters. Although safety and efficacy have been demonstrated in pediatric patients one year and older, safety and effectiveness in infants below the age of one year have not been established.

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.

Dosage and Administration
For Ophthalmic use
The recommended dosage regimen for the treatment of bacterial conjunctivitis is:
Day 1 and 2
Instill one to two drops every two to four hours in the affected eye(s).
Day 3 through 7
Instill one to two drops four times daily.

The recommended dosage regimen for the treatment of bacterial corneal ulcer is:
Day 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.
Day 3 through 7 to 9
Instill one to two drops hourly, while awake.
Days 7 to 9 through treatment completion
Instill one to two drops, four times daily.

For Otic use
Otitis Externa
The recommended dosage regimen for the treatment of otitis externa is:
For pediatric patients (from 1 to 12 years old): five drops (0.25 ml, 0.75 mg Ofloxacin) instilled in to the affected ear twice daily for ten days.

For patients 12 years and older: Ten drops (0.5 ml, 1.5 mg Ofloxacin) instilled into the affected ear twice daily for ten days. The solution should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness that may result from the instillation of a cold solution. The patient should lie with the affected ear up- ward, and then the drops should be instilled. This position should be maintained for five minutes to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear.

Acute Otitis Media in pediatric Patients with Tympanostomy Tubes
The recommended dosage regimen for the treatment of acute otitis media in pediatric patients (from one to 12 years old) with tympanostomy tubes is:
Five drops (0.25 ml, 0.75 mg Ofloxacin) instilled into the affected ear twice daily for ten days. The solution should be warmed by holding the bottle in the hand for one or two minutes to avoid

dizziness, which may result from the instillation of a cold solution. The patient should lie with the affected ear upward, and then the drops should be in- stilled. The tragus should then be pumped 4 times by pushing inward to facilitate penetration of the drops into the middle ear. This position should be maintained for five minutes. Repeat, if necessary, for the opposite ear.

Chronic Suppurative Otitis Media with Perforated Tympanic Membranes
The recommended dosage regimen for the treatment of chronic suppurative otitis media with perforated tympanic membranes in patients 12 years and older is:
Ten drops (0.5 ml, 1.5 mg Ofloxacin) instilled into the affected ear twice daily for fourteen days. The solution should be warmed by holding the bottle in the hand for, one or two minutes to avoid dizziness that may result from the instillation of a cold solution. The patient should lie with the affected ear upward, before instilling the drops. The tragus should then be pumped 4 times by pushing inward to facilitate penetration into the middle ear. This position should be maintained for five minutes.
Repeat, if necessary, for the opposite ear.

Presentation
Dropper bottle of 5 ml