



SCOTT-EDIL PHARMACIA LTD.

56, EPIP, Phase-I, Jharmajri, Baddi-173 205, (HP), India

Summary of Product Characteristics (SPC)

1. Name of the medicinal product

Ofloxacin Eye/Ear Drops

1.1 *International Non-Proprietary Name (INN)*

Ofloxacin Eye/Ear Drops

1.2 *Strength*

0.3% w/v

1.3 *Pharmaceutical form*

Ophthalmic and Otic Solution

2. Qualitative and quantitative composition

Composition:

Ofloxacin USP 0.3% w/v

Benzalkonium Chloride Solution USP 0.02%w/v

Aqueous Buffered Vehicle q.s.

3. Pharmaceutical form

Description: Clear, pale yellow solution is filled in white HDPE vial.

Pharmaceutical form- Ophthalmic and Otic Solution.

4. Clinical particulars

4.1 *Therapeutic indications*

Ofloxacin Eye/Ear Drops is indicated for the topical treatment of external ocular infections (such as conjunctivitis and keratoconjunctivitis) & bacterial Corneal Ulcers in adults and children caused by ofloxacin - sensitive organisms. Safety and efficacy in the treatment of ophthalmia neonatorum has not been established.

4.2 *Posology and method of administration*

Posology:

Topical ocular instillation.

For all ages: one to two drops in the affected eye(s) every two to four hours for the first two days and then four times daily. The length of treatment should not exceed ten days.

The recommended dosage regimen for the treatment of bacterial corneal ulcer is as follows:

Days 1 and 2: Instill one to two drops into the affected eye every 30 minutes, while awake. Awaken at approximately 4 and 6 hours after retiring and instill one to two drops.

Days 3 through 7 to 9: Instill one to two drops hourly, while awake.

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

The length of treatment should not exceed 10 days.

Method of administration

Ocular and otic use.

4.3 Contraindications

It is contra-indicated in individuals who have shown hypersensitivity to ofloxacin, any of its excipients or any other quinolones.

4.4 Special warnings and precautions for use

Ofloxacin Eye/Ear Drops is not for injection.

Safety and effectiveness in infants below the age of one year have not been established.

Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) 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 oedema), airway obstruction, dyspnoea, urticaria, and itching.

If an allergic reaction to Ofloxacin Eye/Ear Drops occurs, discontinue the drug. Use Ofloxacin Eye/Ear Drops with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

When using Ofloxacin Eye/Ear Drops the risk of rhinopharyngeal passage which can contribute to the occurrence and the diffusion of bacterial resistance should be considered. As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms.

If worsening infection occurs, or if clinical improvement is not noted within a reasonable period, discontinue use and institute alternative therapy.

Cardiac disorders

Caution should be taken when using fluoroquinolones, including Ofloxacin Eye/Ear Drops in patients with known risk factors for prolongation of the QT interval such as, for example:

- congenital long QT syndrome
- concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics)
- uncorrected electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia)
- cardiac disease (e.g. heart failure, myocardial infarction, bradycardia)

Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including Ofloxacin Eye/Ear Drops, in these populations.

Use Ofloxacin Eye/Ear Drops with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents.

Data are very limited to establish efficacy and safety of Ofloxacin Eye/Ear Drops eye drops 0.3% in the treatment of conjunctivitis in neonates.

The use of Ofloxacin Eye/Ear Drops in neonates with ophthalmia neonatorum caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* is not recommended as it has not been evaluated in such patients.

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Use in elderly: No comparative data are available with topical dosing in elderly versus other age groups.

Clinical and non-clinical publications have reported the occurrence of corneal perforation in patients with pre-existing corneal epithelial defect or corneal ulcer, when treated with topical fluoroquinolone antibiotics. However, significant confounding factors were involved in many of these reports, including advanced age, presence of large ulcers, concomitant ocular conditions (e.g. severe dry eye), systemic inflammatory diseases (e.g. rheumatoid arthritis), and concomitant use of ocular steroids or non-steroidal anti-inflammatory drugs. Nevertheless, it is necessary to advise caution regarding the risk of corneal perforation when using product to treat patients with corneal epithelial defects or corneal ulcers.

Corneal precipitates have been reported during treatment with topical ophthalmic ofloxacin. However, a causal relationship has not been established.

Long-term, high-dose use of other fluoroquinolones in experimental animals has caused lenticular opacities. However, this effect has not been reported in human patients, nor has it been noted following topical ophthalmic treatment with ofloxacin for up to six months in animal studies including studies in monkeys.

Ofloxacin Eye/Ear Drops contains the preservative benzalkonium chloride which may cause eye irritation, symptoms of dry eyes, and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised.

Use of contact lenses is not recommended in patients receiving treatment for an eye infection. Patients should remove contact lenses prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

Patients should be monitored in case of prolonged use.

Sun or UV-exposition should be avoided during use of ofloxacin due to the potential for photosensitivity.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

It has been shown that the systemic administration of some quinolones inhibits the metabolic clearance of caffeine and theophylline. Drug interaction studies conducted with systemic ofloxacin have demonstrated that metabolic clearance of caffeine and theophylline are not significantly affected by ofloxacin.

Although there have been reports of an increased prevalence of CNS toxicity with systemic dosing of fluoroquinolones when used concomitantly with systemic nonsteroidal anti-inflammatory drugs (NSAIDs), this has not been reported with the concomitant systemic use of NSAIDs and ofloxacin.

Ofloxacin Eye/Ear Drops, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmics, tricyclic antidepressants, macrolides, antipsychotics).

4.6 Pregnancy and lactation

Pregnancy

There have been no adequate and well-controlled studies performed in pregnant women. Since systemic quinolones have been shown to cause arthropathy in immature animals, it is recommended that Ofloxacin Eye/Ear Drops not be used in pregnant women.



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Breast-feeding

Because ofloxacin and other quinolones taken systemically are excreted in breast milk, and there is potential for harm to nursing infants, a decision should be made whether to temporarily discontinue nursing or not to administer the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

Transient blurring of vision may occur on instillation of eye drops. Do not drive or operate hazardous machinery unless vision is clear.

4.8 Undesirable effects

General

Serious reactions after use of systemic ofloxacin are rare and most symptoms are reversible. Since a small amount of ofloxacin is systemically absorbed after topical administration, side-effects reported with systemic use could possibly occur.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The following terminologies have been used in order to classify the occurrence of undesirable effects:

Frequency categories: Very common ($\geq 1/10$); Common ($\geq 1/100$ to $< 1/10$); Uncommon ($\geq 1/1,000$ to $< 1/100$); Rare ($\geq 1/10,000$ to $< 1/1,000$); Very rare ($< 1/10,000$) and not known (cannot be estimated from the available data):

Immune System Disorders

Not Known: Hypersensitivity reaction including signs or symptoms of Eye allergy (such as Eye pruritus and Eyelid pruritus) and Anaphylactic reactions (such as angioedema, dyspnea, anaphylactic shock, oropharyngeal swelling, facial oedema and tongue swollen)

Nervous System Disorders

Not known: Dizziness

Eye Disorders

Common: Eye irritation; Ocular discomfort

Not known: Keratitis; Conjunctivitis; Vision blurred; Photophobia; Eye oedema; Foreign body sensation in eyes; Lacrimation increased; Dry eye; Eye pain; Ocular hyperaemia; Periorbital oedema (including eyelid oedema)

Cardiac disorders

Not known: ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation); ECG QT prolonged (see section 4.4 and 4.9)

Gastrointestinal Disorders

Not known: Nausea

Skin and Subcutaneous Tissue Disorders

Not Known: Stevens-Johnson syndrome; Toxic epidermal necrolysis

4.9 Overdose

In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.



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5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, anti-infectives, fluoroquinolones, ATC code: S01AE01

Ofloxacin is a synthetic fluorinated 4-quinolone antibacterial agent with activity against a broad spectrum of Gram negative and to a lesser degree Gram positive organisms.

Ofloxacin has been shown to be active against most strains of the following organisms both in vitro and clinically in ophthalmic infections. Clinical trial evidence of the efficacy of Ofloxacin Eye/Ear Drops against *S. pneumoniae* was based on a limited number of isolates.

Gram-negative bacteria: *Acinetobacter calcoaceticus* var. *anitratum*, and *A. calcoaceticus* var. *iwoffi*; *Enterobacter* Sp. including *E. cloacae*; *Haemophilis* Sp, including *H. influenza* and *H. aegyptius*; *Klebsiella* Sp., including *K. Pneumoniae*; *Moraxella* Sp., *Morganella morganii*; *Proteus* Sp., including *P. Mirabilis*; *Pseudomonas* Sp.; including *P. Aeruginosa*, *P. cepacia*, and *P. fluorescens*; and *Serratia* Sp., including *S. marcescens*.

Gram-positive bacteria: *Bacillus* Sp.; *Corynebacterium* Sp.; *Micrococcus* Sp.; *Staphylococcus* Sp., including *S. aureus* and *S. epidermidis*; *Streptococcus* Sp., including *S. Pneumoniae* (see above), *S. viridans* and Beta-haemolytic.

The primary mechanisms of action is through inhibition of bacterial DNA gyrase, the enzyme responsible for maintaining the structure of DNA.

Ofloxacin is not subject to degradation by beta-lactamase enzymes nor is it modified by enzymes such as aminoglycoside adenylases or phosphorylases, or chloramphenicol acetyltransferase.

5.2 Pharmacokinetic properties

After ophthalmic instillation, ofloxacin is well maintained in the tear-film.

In a healthy volunteer study, mean tear film concentrations of ofloxacin measured four hours after topical dosing (9.2 µg/g) were higher than the 2µg/ml minimum concentration of ofloxacin necessary to inhibit 90% of most ocular bacterial strains (MIC90) in-vitro.

Maximum serum ofloxacin concentrations after ten days of topical dosing were about 1000 times lower than those reported after standard oral doses of ofloxacin, and no systemic side-effects attributable to topical ofloxacin were observed.

5.3 Preclinical safety data

There are no toxicological safety issues with this product in man as the level of systemic absorption from topical ocular administration of ofloxacin is minimal.

Animal studies in the dog have found cases of arthropathy in weight bearing joints of juvenile animals after high oral doses of certain quinolones. However, these findings have not been seen in clinical studies and their relevance to man is unknown.

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6. Pharmaceutical particulars

6.1 List of excipients

- Benzalkonium Chloride Sodium USP
- Hypromellose USP
- Edetate Disodium USP
- Sodium chloride USP
- Sodium Hydroxide USP
- Water for injection USP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store in a dark place at a temperature not exceeding 25°C.

6.5 Nature and contents of container

10 ml HDPE Vial.

6.6 Special precautions for disposal and other handling

None Known.

7. APPLICANT/MANUFACTURER

Manufactured By:

Scott-Edil Pharmacia Limited,
56, EPIP, Phase-I, Jharmajri,
Baddi, Distt. Solan- 173205 (H.P)
INDIA

Marketed By

Mankind Lifesciences Ltd.,
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