NATIONAL AGENCY FOR FOOD & DRUG ADMINISTRATION & CONTROL (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

Product Name

TRUST TIME OFLOXACIN EYE/EAR DROPS

(Ofloxacin Eye/Ear Drops 0.3% w/v)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product

TRUST TIME OFLOXACIN EYE/EAR DROPS

(Ofloxacin Eye/Ear Drops 0.3% w/v)

2. Qualitative and quantitative composition

Composition:

Ofloxacin USP 0.3% w/v

Benzalkonium Chloride NF 0.01 % w/v

(As Preservative)

Sterile aqueous vehicle q.s.

3. Pharmaceutical form

Eye/Ear Drops

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) in adults and children caused by ofloxacin - sensitive organisms. Safety and efficacy in the treatment of ophthalmia neonatorum has not been established indicated for the treatment of otitis externa.

Ofloxacin otic solution is used to treat infections of the ear canal. It also is used to treat infections of the middle ear in patients with nonintact tympanic membranes (holes or tubes in the eardrums).

4.2 Posology and method of administration

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.

Ear: Ofloxacin is used to treat outer ear infections (swimmer's ear or ear canal infections) and middle ear infections. It works by stopping the growth of bacteria.

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

Days 1 and 2	Instill one to two drops every 2–4 hours in the affected eye(s).
Days 3 through 7	Instill one to two drops four times daily.

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

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

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 occurs, discontinue the drug. Use ofloxacin with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

When using ofloxacin 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 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 anti-arrhythmics, 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, in these populations.

Use ofloxacin 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 drops 0.3% in the treatment of conjunctivitis in neonates.

The use of ofloxacin eye 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.

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 contains the preservative benzalkonium chloride which may cause ocular irritation and discolour soft contact lenses.

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

Use of contact lenses is not recommended in patients receiving treatment for an eye infection.

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, 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

Use in 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 not be used in pregnant women.

Use during lactation: 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, considering 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.

Frequency categories: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥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

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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, anti-infectives, fluoroquinolones

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 organism.

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 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. fluoroscens; 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 , 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.

6. Pharmaceutical particulars

6.1 List of excipients.

Benzalkonium Chloride (50% Solution) NF
Sodium Metabisulphite BP
E.D.T. A. Sodium BP
Boric Acid BP
Borax BP
Acetic Acid BP
Water For Injection BP

6.2 Incompatibilities

Not Known

6.3 Shelf life

36 months Unopened

1 month once opened

Use the solution within one month after first opening the container.

6.4 Special precautions for storage

Store at temperature below 30°C. Protect from light.

6.5 Nature and contents of container

10 ml plastic vial with duly sealed screw capped.

6.6 Special precautions for disposal and other handling

1. If irritation persists or increases, discontinue the use and consult physician.
2. Do not touch the dropper tip or other dispensing tip to any surface since this may contaminate the solution.

   Screw the cap tightly to pierce the nozzle seal.

7. Manufacturer Name

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8. Marketing Authority

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