Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

ZO Eye Drops (Ofloxacin Ophthalmic Solution USP 0.3% w/v).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Ofloxacin …….....…. 0.3% w/v.
Benzalkonium Chloride …….……..... 0.005% w/v.
(as preservative)
Aqueous Vehicle…….…….. q.s.

3. PHARMACEUTICAL FORM

Eye drops, ophthalmic solution.

Description

Light yellow colour, clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

ZO Eye Drops is indicated for the topical treatment of external ocular infections (such as conjunctivitis and keratoconjunctivitis) in adults and children.

4.2 Posology and Method of Administration

Topical ocular instillation.

Adults and children above 1 year: 1 to 2 drops in the affected eye(s) every 2 to 4 hours for the first 2 days and then four times daily. Duration of treatment should not exceed 10 days.
Or, as directed by Physician.

Paediatric Population

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

Method of Administration

- For ocular use only.
- Not for injection.
- Do not touch tip of the vial to finger or to eye(s)/eyelids or to any other surface since this may contaminate the solution.
- If eye irritation occurs, discontinue the use and consult the Physician.
- Contact lenses should be removed before instillation of the eye drops and may be reinserted after 15 minutes.
- If more than one topical ophthalmic medicinal product is being used, the medicinal products should be instilled 5 to 15 minutes apart. Eye ointments should be administered last.
- Discard unused portion of eye drop, if any, after one month of first opening the vial (even though expiry date is longer).
- Follow the directions mentioned on the container label.

4.3 Contraindications

ZO Eye Drops are contraindicated in patient with known hypersensitivity to the ofloxacin or to any other quinolone or to any of the excipients listed in section 6.1.

4.4 Special Warnings and Precautions for Use

Hypersensitivity: 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 this medicinal product occurs, discontinue the use. Use ZO Eye Drops with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

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

Bacterial Resistance: When using ZO Eye Drops the risk of rhinopharyngeal passage which can contribute to the occurrence and the diffusion of bacterial resistance should be considered. As with other antiinfectives, 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 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 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.

Clinical and non-clinical data 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 (NSAIDs). 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 Usage: 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 6 months in animal studies including studies in monkeys. As a caution, patients should be monitored in case of prolonged usage.

Benzalkonium Chloride (BKC) as Preservative: Benzalkonium chloride is used as preservative in this product which has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. This medicinal product should be used with caution in dry eye patients and in patients where the cornea may be compromised.

From the limited data available, there is no difference in the adverse event profile in children compared to adults. However, eyes in children generally show a stronger reaction for a given stimulus than the adult eye. Irritation may have an effect on treatment adherence in children.
Contact Lenses: Contact lenses may absorb benzalkonium chloride and these should be removed before instilling this eye drops but may be reinserted after 15 minutes.

Paediatric Population
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 ZO 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.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction
No interaction studies have been performed with ofloxacin ophthalmic solution.
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 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 Fertility, 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 ZO Eye Drops not be used in pregnant women.

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.

Fertility
In animal studies, ofloxacin has no effect on fertility. No human data is available.

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

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 (≥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):

Organ System Disorder	**Common**	**Rare**	**Not Known**
Immune System Disorders			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 swollen tongue).
Nervous System Disorders			Dizziness.
Eye Disorders	Eye irritation; Ocular discomfort.		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			Ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation); ECG QT prolonged.
Gastrointestinal Disorders			Nausea.
Skin and Subcutaneous Tissue Disorders			Stevens-Johnson syndrome (SJS); Toxic epidermal necrolysis (TEN).

Reporting of Suspected Adverse Reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

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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, antiinfectives, fluoroquinolones. **ATC Code:** S01AE01.

Mechanism of Action

This medicinal product contains ofloxacin, a broad-spectrum anti-infective agent that belongs to the fluoroquinolones group. Ofloxacin is bactericidal in nature and acts on both Gram-positive and Gram-negative bacteria. The primary mechanisms of action are through inhibition of bacterial DNA gyrase, the enzyme required for DNA synthesis (replication, transcription, repair, and recombination). Ofloxacin thereby prevents bacterial cell division and kills the bacteria.

Pharmacodynamic Effects / Microbiology

Ofloxacin is a synthetic fluorinated 4-quinolone antibacterial agent with activity against a broad spectrum of Gram negative and to 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 drops against *S. pneumoniae* was based on a limited number of isolates.

Gram-negative bacteria: *Acinetobacter calcoaceticus* and *A. lwoffi*; 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.

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 4 hours after topical dosing (9.2 µg/g) were higher than the 2 µg/ml minimum concentration of ofloxacin necessary to inhibit 90% (MIC_{90}) of most ocular bacterial strains *in-vitro*.

Maximum serum ofloxacin concentrations after 10 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 medicinal 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

Sodium Chloride, Benzalkonium Chloride, Hydrochloric acid, Sodium Hydroxide pellets, Water for Injection.

6.2 Incompatibilities
Not Available.

6.3 Shelf-life
24 months.

6.4 Special Precautions for Storage
Store at temperature not exceeding 25 °C. Protect from light.

6.5 Nature and Contents of Container
5ml labelled LDPE vial with HIPS cap, packed in a carton with pack insert.

6.6 Special Precautions for Disposal and Other Handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Registered Office

Name: FDC Limited
Address: B- 8, MIDC Industrial Area, Waluj, Aurangabad- 431 136, Maharashtra
Phone : 022-26739-273
Fax : 022-26300614
E-mail: tripti.nakhare@fdcindia.com

8. MARKETING AUTHORISATION NUMBER(S)

Certificate No: 07166/08309/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Mar 4, 2022

10. DATE OF REVISION OF THE TEXT

September 2023.