1.3.1 :SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

ZOEYE (Ofloxacin Ophthalmic Solution USP 0.3 % w/v)

1.1 Strength : 0.3%

1.2 Pharmaceutical form : Eye Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:
Ofloxacin USP ……..0.3% w/v
Benzalkonium Chloride
(As preservative) USP/NF….0.005% w/v
Aqueous Vehicle……q.s.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye drops, solution

Description: Light yellow colour, clear solution

pH: Between 6.3 to 6.5

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Ocular use: The preparation is indicated for the treatment of bacterial conjunctivitis and bacterial corneal ulcers caused by susceptible strains of bacteria.
Otic: The prearation is indicated for the treatment of Otitis externa , chronic supprative otitis media and acute otitits media

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

4.3 Contra-indications

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 ophthalmic solution 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 ophthalmic solution occurs, discontinue the drug.

Use Ofloxacin ophthalmic solution with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

When using Ofloxacin ophthalmic solution, 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.

<u>Cardiac disorders</u>

Caution should be taken when using fluoroquinolones, including Ofloxacin ophthalmic solution 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 ophthalmic solution, in these populations.

Use Ofloxacin ophthalmic solution with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents.

Data are very limited to establish efficacy and safety of Ofloxacin ophthalmic solution 0.3% in the treatment of conjunctivitis in neonates.

The use of Ofloxacin ophthalmic solution 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 ophthalmic solution 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 ophthalmic solution, 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 ophthalmic solution 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, 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.

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

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.

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
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 ophthalmic solution 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 (MIC_{90}) 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

Sr. No.	Ingredient
1	Ofloxacin
2	Sodium Chloride
3	Benzalkonium Chloride
4	Hydrochloric Acid
5	Sodium Hydroxide
6	Water for Injection

6.2. Incompatibilities

Not Available

6.3. Shelf life

24 months

6.4. Special Precautions for Storage

The product should be used no longer than 28 days after first opening the container.

6.5. Nature and contents of container:

5ml of solution filled in 5 ml labeled translucent LDPE bottle with insert cap assembly comprising of a tan colored screw cap over a LDPE nozzle with tamper evident LDPE dust cover sealing the bottle cap. One such bottle is packed in a carton with pack insert.

6.6. Special precautions for disposal and other handling

Not Applicable

7. Applicant/Manufacturer:

FDC Limited
B-8, MIDC Industrial Area, Waluj, Aurangabad- 432236,
Maharashtra, India.