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

Registration & Regulatory Affairs (R & R) Directorate

Product Name

EYECIPRO
(CIPROFLOXACIN EYE DROPS 0.3% W/V)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. Name of the medicinal product

EYECIPRO

(Ciprofloxacin Eye Drops 0.3% w/v)

2. Qualitative and quantitative composition

Composition :

Ciprofloxacin Hydrochloride BP	
Eq. to Ciprofloxacin	0.3% w/v
Benzalkonium Chloride BP	0.01% w/v
(as preservative)	
Sterile aqueous vehicle	q.s.

3. Pharmaceutical form

Eye Drops

4. Clinical particulars

4.1 Therapeutic indications

Adults, newborn infants (0-27 days), infants and toddlers (28 days to 23 months), children (2-11 years) and adolescents (12-16 years).

Ciprofloxacin Eye Drops is indicated for the treatment of corneal ulcers and superficial infections of the eye and adnexa caused by susceptible strains of bacteria. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Adults, newborn infants (0-27 days), infants and toddlers (28 days to 23 months), children (2-11 years) and adolescents (12-16 years).

Corneal Ulcers: Ciprofloxacin intervals, even during night time: On the first day, instil 2 drops into the affected eye every 15 minutes for the first six hours and then 2 drops into the affected eye every 30 minutes for the remainder of the day.

On the second day, instil 2 drops in the affected eye hourly.

On the third through the fourteenth day, place two drops in the affected eye every 4 hours. If the patient needs to be treated longer than 14 days, the dosing regimen is at the discretion of the attending physician

Superficial Ocular Infection: The usual dose is one or two drops in the affected eye(s) four times a day. In severe infections, the dosage for the first two days may be one or two drops every two hours during waking hours. For either indication a maximum duration of therapy of 21 days is recommended. The dosage in children above the age of 1 year is the same as for adults.

Use in children Safety and effectiveness of Ciprofloxacin Eye Drops were determined in 230 children between the ages of 0 and 12 years of age. No serious adverse drug reaction was reported in this group of patients.

Use in renal and hepatic impairment No studies have been performed using Ciprofloxacin Eye Drops in patients with kidney or liver problems.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in
- Hypersensitivity to quinolones.

4.4 Special warnings and precautions for use

After cap is removed, if tamper evident snap collar is loose, remove before using product.

For Ocular use only.

The clinical experience in children less than one year old, particularly in neonates is very limited. The use of Ciprofloxacin Eye Drops in neonates with ophthalmia neonatorum of gonococcal or chalamydial origin is not recommended as it has not been evaluated in such patients. Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition. When using Ciprofloxacin Eye Drops one should take into account the risk of rhinopharyngeal passage which can contribute to the occurrence and the diffusion of bacterial resistance. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, were observed in patients receiving treatment based on systematically administered quinolones. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnoea, urticaria and itching. Only a few patients had a history of hypersensitivity reactions

Serious acute hypersensitivity reactions to ciprofloxacin may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated.

Ciprofloxacin Eye Drops should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity. As with all antibacterial preparations prolonged

use may lead to overgrowth of non-susceptible bacterial strains or fungi. If superinfection occurs, appropriate therapy should be initiated. Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including ciprofloxacin, particularly in elderly patients and those treated concurrently with corticosteroids. Therefore, treatment with Ciprofloxacin Eye Drops should be discontinued at the first sign of tendon inflammation.

In patients with corneal ulcer and frequent administration of Ciprofloxacin Eye Drops, white topical Ocular precipitates (medication residue) have been observed which resolved after continued application of Ciprofloxacin Eye Drops. The precipitate does not preclude the continued application of Ciprofloxacin Eye Drops nor does it adversely affect the clinical course of the recovery process. The onset of the precipitate was within 24 hours to 7 days after starting therapy. Resolution of the precipitate varied from immediately to 13 days after therapy commencing. Contact lens wear is not recommended during treatment of an Ocular infection. Therefore, patients should be advised not to wear contact lenses during treatment with Ciprofloxacin Eye Drops contains benzalkonium chloride which may cause irritation and is known to discolour soft contact lenses.

Avoid contact with soft contact lenses. In case patients are allowed to wear contact lenses they should be instructed to remove them prior to application of Ciprofloxacin Eye Drops and wait at least 15 minutes before reinsertion.

4.5 Interaction with other medicinal products and other forms of interaction

Specific drug interaction studies have not been conducted with ophthalmic ciprofloxacin. Given the low systemic concentration of ciprofloxacin following topical Ocular administration of the product, drug interactions are unlikely to occur. If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.6 Fertility, pregnancy and lactation

Fertility

Studies have not been performed in humans to evaluate the effect of topical administration of ciprofloxacin on fertility. Oral administration in animals does not indicate direct harmful effects with respect to fertility.

Pregnancy

There are no adequate data from the use of Ciprofloxacin Eye Drops in pregnant woman. Animal studies do not indicate direct harmful effects with respect to

reproductive toxicity. Systemic exposure to ciprofloxacin after topical use is expected to be low. As a precautionary measure, it is preferable to avoid the use of Ciprofloxacin Eye Drops during pregnancy, unless the therapeutic benefit is expected to outweigh the potential risk to the fetus.

Breastfeeding

Orally administered ciprofloxacin is excreted in the human milk. It is unknown whether ciprofloxacin is excreted in human breast milk following topical Ocular administration. A risk to the suckling child cannot be excluded. Therefore, caution should be exercised Ciprofloxacin Eye Drops is administered to nursing women.

4.7 Effects on ability to drive and use machines

This product has no or negligible influence on the ability to drive or use machines. Temporarily blurred vision or other visual disturbances may affect the ability to drive or use machines. If transient blurred vision occurs upon instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

In clinical trials, the most frequently reported adverse drug reactions were Ocular discomfort, dysgeusia and corneal deposits occurring approximately in 6%, 3% and 3% of patients respectively.

Tabulated summary of adverse reactions. The adverse reactions listed below are classified according to the following convention: 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), or not known (cannot be estimated from the available data). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions have been observed during clinical trials and post-marketing experience.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group – Ophthalmologicals, Other Antiinfectives.

ATC Code: S01AX13

Mechanism of Action**:** Ciprofloxacin Eye Drops, solution contains the fluoroquinolone ciprofloxacin. The cidal and inhibitory activity of ciprofloxacin against bacteria results from an interference with the DNA gyrase, an enzyme needed by the bacterium for the synthesis of DNA. Thus the vital information from the bacterial chromosomes cannot

be transcribed which causes a breakdown of the bacterial metabolism. Ciprofloxacin has in vitro activity against a wide range of Gram-positive and Gram-negative bacteria.

Mechanism of Resistance

Fluoroquinolone resistance, particularly ciprofloxacin, requires significant genetic changes in one or more of five major bacterial mechanisms: a) enzymes for DNA synthesis, b) protecting proteins, c) cell permeability, d) drug efflux, or e) plasmid-mediated aminoglycoside 6'-N-acetyltransferase, AAC (6')-Ib. Fluoroquinolones, including ciprofloxacin, differ in chemical structure and mode of action from aminoglycosides, β-lactam antibiotics, macrolides, tetracyclines, sulfonamides, trimethoprim, and chloramphenicol. Therefore, organisms resistant to these drugs may be susceptible to ciprofloxacin.

Breakpoints:

There are no official topical Ocular break points for ciprofloxacin and although systemic breakpoints have been used, their relevance to topical therapy is doubtful. The EUCAST clinical MIC breakpoints used for this antibiotic are the following:

Staphylococcus species	S ≤ 1mg/l, R ≥ 1mg/l
Streptococcus pneumoniae	S ≤ 0.125mg/l, R ≥ 2mg/l
Haemophilus influenzae	S ≤ 0.5mg/l, R ≥ 0.5mg/l
Moraxella catarrhalis	S ≤ 0.5mg/l, R ≥ 0.5mg/l
Pseudomonas aeruginosa	S ≤ 0.5mg/l, R ≥ 1mg/l

Susceptibility to Ciprofloxacin:

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable. The presentation below lists bacterial species recovered from external Ocular infections of the eye

Commonly susceptible species

Aerobic Gram-positive microorganisms

Corynebacterium accolens

Corynebacterium auris

Corynebacterium propinquum

Corynebacterium psudodiphtheriticum

Corynebacterium striatum

Staphylococcus aureus (methicillin susceptible - MSSA)

Staphylococcus capitis

Staphylococcus epidermidis (methicillin susceptible - MSSE)

Staphylococcus hominis

Staphylococcus saprophyticus

Staphylococcus warneri

Streptococcus pneumonia

Streptococcus viridans Group

Aerobic Gram-negative microorganisms

Acinetobacter species

Haemophilus influenza

Moraxella catarrhalis

Pseudomonas aeruginosa

Serratia marcescens

Species for which acquired resistance may be a problem

Aerobic Gram-positive micro-organisms:

Staphylococcus aureus (methicillin resistant - MRSA)

Staphylococcus epidermidis (methicillin resistant - MRSE)

Staphylococcus lugdunensis

Aerobic Gram-negative micro-organisms:

None

Other micro-organisms:

None

5.3 Toxicology

Oral, mouse: LD_{50} = 1500 mg/kg; Oral, rat: LD_{50} = 2500 mg/kg. Toxic reactions including fatalities have occurred in the premature and newborn; the signs and symptoms associated with these reactions have been referred to as the gray syndrome. Symptoms include (in order of appearance) abdominal distension with or without emesis, progressive pallid cyanosis, vasomotor collapse frequently accompanied by irregular respiration, and death within a few hours of onset of these symptoms.

6. Pharmaceutical particulars

6.1 List of excipients

- Benzalkonium Chloride Solution BP
- Sodium Chloride BP
- Disodium Edetate BP

- Disodium Hydrogen Phosphate BP
- Sodium Hydroxide BP
- Water for Injection BP

6.2 Incompatibilities

None known

6.3 Shelf life

36 months Unopened

6.4 Special precautions

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

6.5 Nature and contents of container

10 ml vial.

6.6 Instruction for use handling and disposal:

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.

7. Manufacturer name

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8. Marketing Authority

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