1.5 PRODUCT INFORMATION

1.5.1 PRESCRIBING INFORMATION
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT – CIPRO EYE

CIPROFLOXACIN OPHTHALMIC SOLUTION USP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Ciprofloxacin Hydrochloride USP
Eq. to Ciprofloxacin …….0.3%w/v
Benzalkonium Chloride NF…..0.01%w/v
(As Preservative)

3. PHARMACEUTICAL FORM

Eye/ Ear Drops

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

EYE: Ciprofloxacin Ophthalmic solution 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.

EAR: Otitic externa, acute otitic media, chronic suppurative otitic media, Prophylaxis in otic surgeries such as mastoid surgery.

4.2 Posology and Method of Administration

EYE: 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 Ophthalmic solution must be administered in the following intervals, even during night time:

On the first day, instill 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, instill 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 Ophthalmic solution 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.

EAR: For all infections 2 to 3 drops every two to three hours. Initially reducing frequency of instillation with control of infection.

4.3 Contraindications:

Hypersensitivity to quinolones or any component of this medication.

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.

4.6 Pregnancy and Lactation

There are no adequate data from the use of Ciprofloxacin Ophthalmic solution 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 Opthalmic solution during pregnancy, unless the therapeutic benefit is expected to outweigh the potential risk to the fetus.
It is unknown whether ciprofloxacin is excreted in human breast milk following topical ocular or otic administration.

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.

The following undesirable effects were reported in association with the ophthalmic use of Ciprofloxacin Eye/ Ear Drops:

System Organ Classification	MedDRA Preferred Term (v. 15.1)
Immune system disorders	*Rare:* hypersensitivity
Nervous system disorders	*Uncommon:* headache *Rare:* dizziness

Eye disorders	*Common*: corneal deposits, ocular discomfort, ocular hyperaemia *Uncommon*: keratopathy, punctate keratitis, corneal infiltrates, photophobia, visual acuity reduced, eyelid oedema, blurred vision, eye pain, dry eye, eye swelling, eye pruritus, lacrimation increased, eye discharge, eyelid margin crusting, eyelid exfoliation, conjunctival oedema, erythema of eyelid *Rare:* ocular toxicity, keratitis, conjunctivitis, corneal epithelium defect, diplopia, hypoaesthesia eye, asthenopia, eye irritation, eye inflammation, hordeolum
Ear and labyrinth disorders	*Rare:* ear pain
Respiratory, thoracic and mediastinal disorders	*Rare:* paranasal sinus hypersecretion, rhinitis
Gastrointestinal disorders	*Common:* dysgeusia *Uncommon*: nausea *Rare:* diarrhoea, abdominal pain
Skin and subcutaneous tissue disorders	*Rare*: dermatitis
Musculoskeletal and connective tissue disorders	*Not known:* tendon disorder

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Mechanism of Action

Ciprofloxacin Opthalmic 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.

5.2 Pharmacokinetic Properties

Ciprofloxacin Opthalmic solution , is rapidly absorbed into the eye following topical ocular administration. Systemic levels are low following topical administration. Plasma levels of ciprofloxacin in human subjects following 2 drops of 0.3% ciprofloxacin solution every 2 hours for two days and then every four hours for 5 days ranged from non-quantifiable (<1.0 ng/mL) to 4.7 ng/mL. The mean peak ciprofloxacin plasma level obtained in this study is approximately 450-fold less than that seen following a single oral dose of 250 mg ciprofloxacin. The systemic pharmacokinetic properties of ciprofloxacin have been well studied. Ciprofloxacin widely distributes to tissues of the body. The apparent volume of distribution at steady state is 1.7 to 5.0 l/kg. Serum protein binding is 20-40%. The half-life of ciprofloxacin in serum is 3-5 hours. Both ciprofloxacin and its four primary metabolites are excreted in urine and faeces. Renal clearance accounts for approximately two-thirds of the total serum clearance with biliary and faecal routes accounting for the remaining percentages. In patients with impaired renal function, the elimination half-life of ciprofloxacin is only moderately increased due to extrarenal routes of elimination. Similarly, in patients with severely reduced liver function the elimination half-life is only slightly longer.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients:

Benzalkonium Chloride, Disodium EDTA, Sodium chloride and Water for Injection are used as excipients in the manufacturing process of Ciprofloxacin Eye/Ear Drops.

6.2 Shelf Life

24 months.

6.3 Special Precautions for Storage

Do not store above 30°C. Protect from light.
Keep all medicines out of the reach and sight of children.

6.4 Nature and Contents of Container

5ml LDPE bottle

7. MARKETING AUTHORISATION HOLDER

Ciron Drugs & Pharmaceuticals Pvt. Ltd.
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8. MARKETING AUTHORISATION NUMBER(S)

None

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not applicable