Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Ciprodol 0.3% w/v eye ointment

2. Qualitative and quantitative composition

Ciprofloxacin 0.3% w/v (as hydrochloride).
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Sterile eye ointment

White soft mass filled in a collapsible tube

4. Clinical particulars

4.1 Therapeutic indications

CIPRODOL is indicated for the treatment of corneal ulcers and superficial infections of the eye and adnexa caused by susceptible strains of bacteria.
CIPRODOL (ciprofloxacin ophthalmic ointment) is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the microorganisms listed below:
Gram-Positive:
Staphylococcus aureus,
Staphylococcus epidermidis,
Streptococcus pneumoniae,
Streptococcus Viridans Group
Gram-Negative:
Haemophilus influenzae
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology
Apply a 1/2" ointment ribbon into the conjunctival sac 3 times a day on the first 2 days, then apply a 1/2" ointment ribbon 2 times a day for the next 5 days.
Use in elderly
Clinical studies have indicated dosage modifications are not required for the elderly.
Use in children
Safety and effectiveness of CILOXAN Eye Ointment in pediatric patients below the age of two years have not been established.
Use in patients with hepatic or renal impairment
No studies have been performed using ciprofloxacin 3 mg/g eye ointment in patients with kidney or liver problems.

Method of administration

For ocular use.

To prevent contamination of the tube tip and ointment, care must be taken not to touch the eyelids,surrounding areas or other surfaces with the tube tip. Keep the tube tightly closed when not in use.

If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.
Hypersensitivity to quinolones.

4.4 Special warnings and precautions for use

FOR TOPICAL OPHTHALMIC USE ONLY.NOT FOR INJECTION INTO THE EYE.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose were observed in patients receiving treatment based on systemically administered quinolone. 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. Ciprofloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity reaction.

Serious acute hypersensitivity reactions to ciprofloxacin may require immediate emergency treatment. Epinephrine and other resuscitation measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management should be administered where clinically indicated.

As with other antibacterial preparations, prolonged use may lead to overgrowth of non-susceptible bacterial strains or fungi. If superinfection occurs, appropriate therapy should be initiated.

Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit lamp bio microscopy and, where appropriate, fluorescein staining.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including ciprofloxacin, particularly in elderly patients and in those treated concurrently with corticosteroids.

Therefore, treatment with CIPRODOL eye ointment should be discontinued at the first sign of tendon inflammation.

In patients with corneal ulcer and frequent administration of CIPRODOL eye ointment, white topical ocular precipitates (medication residue) have been observed which resolved after continued application of CIPRODOL eye ointment. The precipitate does not preclude the continued application of CIPRODOL eye ointment, nor does it adversely affect the clinical course of the recovery process.

Eye Ointments may retard corneal healing and cause visual blurring.

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 CIPRODOL eye ointment.

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

Pregnancy:

In rabbits, as with most antimicrobial agents, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion.

There are no or limited amount of data from the use of CIPRODOL eye ointment in pregnant women.

Animal studies with ciprofloxacin do not indicate direct harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of CIPRODOL eye ointment during pregnancy

Breast-feeding:

Ciprofloxacin is excreted in human milk after its oral administration. It is known that orally administered ciprofloxacin is excreted in the milk of lactating rats. It is unknown whether ciprofloxacin is excreted to human milk following topical ocular administration. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue or abstain from CIPRODOL eye ointment therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

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.

Although ciprofloxacin and other quinolones may cause arthropathy in immature animals after oral administration, topical ocular administration of ciprofloxacin to immature animals did not cause any arthropathy and there is no evidence that the ophthalmic dosage form has any effect on the weight bearing joints.

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 CILOXAN:

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

Description of selected adverse events

With locally applied fluoroquinolones (generalized) rash, toxic epidermolysis, dermatitis exfoliative, Stevens-Johnson syndrome and urticaria occur very rarely.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving

systemic quinolone therapy (see section 4.4). Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnoea, urticaria, and itching.

Ruptures of the shoulder, hand, Achilles, or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and post marketing experience with systemic fluoroquinolones indicate that the risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress, including the Achilles tendon. To date, clinical and post marketing data have not demonstrated a clear association between CILOXAN and musculoskeletal and connective tissue adverse reactions.

In isolated cases blurred vision, decreased visual acuity and medication residue have been observed with ophthalmic ciprofloxacin (see section 4.4).

Moderate to severe phototoxicity has been observed in patients treated with systemic quinolones. Nevertheless, phototoxic reactions to ciprofloxacin are uncommon.

Paediatric population

Safety and effectiveness of CILOXAN 3mg/ml 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.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

A topical overdose of CIPRODOL may be rinsed out from the eye(s) with lukewarm tap water. Due to the characteristics of this preparation no toxic effects are to be expected with an ocular overdose of this product, or in the event of accidental ingestion of the contents of one bottle.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group – Ophthalmologicals, Other Antiinfectives.

ATC Code: S01A X13.

Mechanism of Action

CILOXAN 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 breakpoints 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.

5.2 Pharmacokinetic properties

CIPRODOL eye drops, 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.

There are no pharmacokinetic data available in respect of use in children.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential. Non-clinical developmental toxicity was observed only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use.

6. Pharmaceutical particulars

6.1 List of excipients

Liquid paraffin
Microcrystalline wax
Woolfat
White soft parafin

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage:

Store below 25°C in a dry place.

6.5 Nature and contents of container

3gm of Alu tube packed in a carton along with package insert.

6.6 Special precautions for disposal and other handling:

No special requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:
Dolopharma Healthcare Ltd
Manufacturing site address:
CURIS LIFESCIENCES PVT LTD,
Plot No.Pf/23, Near Acme Pharma, Opp:
Teva Pharma, Sanand, Gidc-Ii, Sananad, Ahmedabad-382110,
Gujarat, India

8. Marketing authorization number

H2024/CTD10245/21877

9. Date of first registration
28/02/2024

10. Date of revision of the text:
November 2024