Streptococcus Viridans Group

Gram-Negative:
Haemophilus influenzae

CONTRAINDICATIONS:
A history of hypersensitivity to ciprofloxacin or any other component of the medication is a contraindication to its use. A history of hypersensitivity to other quinolones may also contraindicate the use of ciprofloxacin.

WARNINGS:
FOR TOPICAL OPHTHALMIC USE ONLY.
NOT FOR INJECTION INTO THE EYE.
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial edema, dyspnea, urticaria, and itching. Only a few patients had a history of hypersensitivity reactions. Serious anaphylactic reactions require immediate emergency treatment with epinephrine and other resuscitation measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

PRECAUTIONS:
General: As with other antibacterial preparations, prolonged use of ciprofloxacin may result in overgrowth of nonsusceptible organisms, including 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 biomicroscopy and, where appropriate, fluorescein staining.

Ciprofloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity reaction.

Ophthalmic ointments may retard corneal healing and cause visual blurring.

Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information For Patients: Do not touch tip to any surface as this may contaminate the ointment.

Drug Interactions: Specific drug interaction studies have not been conducted with ophthalmic ciprofloxacin. However, the systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, enhance the effects of the oral anticoagulant, warfarin, and its derivatives, and has been associated with transient elevations in serum creatinine in patients receiving cyclosporine concomitantly.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
Eight *in vitro* mutagenicity tests have been conducted with ciprofloxacin and the test results are listed below:

Salmonella/Microsome Test (Negative)
E. coli DNA Repair Assay (Negative)

Mouse Lymphoma Cell Forward Mutation Assay (Positive)
Chinese Hamster V79 Cell HGPRT Test (Negative)
Syrian Hamster Embryo Cell Transformation Assay (Negative)
Saccharomyces cerevisiae Point Mutation Assay (Negative)
Saccharomyces cerevisiae Mitotic Crossover and Gene Conversion Assay (Negative)
Rat Hepatocyte DNA Repair Assay (Positive)

Thus, two of the eight tests were positive, but the results of the following three *in vivo* test systems gave negative results:

Rat Hepatocyte DNA Repair Assay
Micronucleus Test (Mice)
Dominant Lethal Test (Mice)

Long term carcinogenicity studies in mice and rats have been completed. After daily oral dosing for up to two years, there is no evidence that ciprofloxacin had any carcinogenic or tumorigenic effects in these species.

Pregnancy: Pregnancy Category C. Reproduction studies have been performed in rats and mice at doses up to six times the usual daily human oral dose and have revealed no evidence of impaired fertility or harm to the fetus due to ciprofloxacin. 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. No teratogenicity was observed at either dose. After intravenous administration, at doses up to 20 mg/kg, no maternal toxicity was produced and no embryotoxicity or teratogenicity was observed. There are no adequate and well controlled studies in pregnant women. CILOXAN (ciprofloxacin hydrochloride ophthalmic ointment) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether topically applied ciprofloxacin is excreted in human milk. However, it is known that orally administered ciprofloxacin is excreted in the milk of lactating rats and oral ciprofloxacin has been reported in human breast milk after a single 500 mg dose. Caution should be exercised when CILOXAN (ciprofloxacin hydrochloride ophthalmic ointment) is administered to a nursing mother.

Pediatric Use: Safety and effectiveness of CILOXAN (ciprofloxacin hydrochloride ophthalmic ointment) 0.3% in pediatric patients below the age of two years have not been established. Although ciprofloxacin and other quinolones may cause arthropathy in immature Beagle dogs 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.

Geriatric Use: No overall clinical differences in safety or effectiveness have been observed between the elderly and other adult patients.

ADVERSE REACTIONS:
The following adverse reactions (incidences) were reported in 2% of the patients in clinical studies for CILOXAN (ciprofloxacin hydrochloride ophthalmic ointment): discomfort, keratopathy. Other reactions associated with ciprofloxacin therapy occurring in less than 1% of patients included allergic reactions, blurred vision, corneal staining, decreased visual acuity, dry eye, edema, epitheliopathy, eye

pain, foreign body sensation, hyperemia, irritation, keratoconjunctivitis, lid erythema, lid margin hyperemia, photophobia, pruritus, and tearing.
Systemic adverse reactions related to ciprofloxacin therapy occurred at an incidence below 1% and included dermatitis, nausea and taste perversion.

DOSAGE AND ADMINISTRATION:
Apply a ½" ribbon into the conjunctival sac three times a day on the first two days, then apply a ½" ribbon two times a day for the next five days.

How Supplied : 3.5 g STERILE ointment supplied in an aluminum tube with a white polyethylene tip and white tamper evident cap. 3.5g - **NDC** 0065-0654-35

Storage: Store at 36°F- 77°F (2°C - 25°C)

ANIMAL PHARMACOLOGY:
Ciprofloxacin and related drugs have been shown to cause arthropathy in immature animals of most species tested following oral administration. However, a one-month topical ocular study using immature Beagle dogs did not demonstrate any articular lesions.

Rx only.
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