SCHEDULING STATUS

Schedule 4

PROPRIETARY NAME AND DOSAGE FORM

EXOCIN® Ophthalmic Solution (Eye Drops)

COMPOSITION

EXOCIN® Ophthalmic Solution contains:

Ofloxacin 3,0 mg/ml

Preservative: Benzalkonium chloride 0,005 % m/v

Other ingredients are sodium chloride and purified water.

PHARMACOLOGICAL CLASSIFICATION

A. 15.1 Ophthalmic preparations with antibiotics.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

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 is bacteriocidal at concentrations equal to or slightly greater than inhibitory concentrations.

The primary mechanism of action is through inhibition of bacterial DNA gyrase, the enzyme responsible for maintaining the structure of DNA.

Ofloxacin possesses an additional bacteriocidal mechanism, which is not dependent on protein or RNA synthesis. It is bacteriocidal in both replicating and non-replicating stages of bacterial growth.

Cross-resistance has been observed between ofloxacin and other fluoroquinolones.

The safety and effectiveness of ofloxacin in treating ophthalmologic infections due to the following microorganisms have not been established in adequate and well-controlled clinical trials:

Aerobes, Gram-Positive

Enterococcus faecalis
Listeria monocytogenes
Staphylococcus capitis
Streptococcus pyogenes
Streptococcus mitis
Staphylococcus simulans
Staphylococcus hominus

Aerobes, Gram-Negative

Acinetobacter calcoaceticus var. anitratum
Acinetobacter calcoaceticus var. wolffii
Citrobacter diversus
Citrobacter freundii
Enterobacter aerogenes
Enterobacter agglomerans
Escherichia coli
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumonia
Moraxella (branhameila) catarrhalis
Moraxella lacunata
Morganella morganii
Neisseria gonorrhoeae
Pseudomonas acidovorans
Pseudomonas fluorescens
Shigella sonnei

Other

Chlamydia trachomatis

Pharmacokinetic properties

Systemic absorption of ofloxacin was detected following ocular administration. In man, the systemic absorption of ofloxacin was in the low ng/ml range.

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 2 µg/g minimum concentration of ofloxacin necessary to inhibit 90 % of most ocular bacterial strains (MIC_{90}) *in vitro*.

INDICATIONS

EXOCIN® is indicated for the topical treatment of external ocular infections caused by ofloxacin susceptible bacteria.

CONTRAINDICATIONS

EXOCIN® is contraindicated in patients hypersensitive to ofloxacin or any of its components. Since systemic quinolones have been shown to cause arthropathy in immature animals, it is recommended that EXOCIN® not be used by pregnant or lactating women (see 'PREGNANCY AND LACTATION'). Safety and effectiveness in infants below the age of one year have not been established (see 'WARNINGS AND SPECIAL PRECAUTIONS').

WARNINGS AND SPECIAL PRECAUTIONS

EXOCIN® is not for injection.

Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions, some following the first dose, have been reported in patients receiving systemic 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 EXOCIN® occurs, discontinue the product and contact your physician. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated. Use EXOCIN® with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents.

When using EXOCIN® eye drops the risk of rhinopharyngeal passage, which can contribute the occurrence and the diffusion of bacterial resistance, should be considered. Prolonged use may result in overgrowth of non-susceptible organisms. If superinfection occurs, or if clinical improvement is not noted within a reasonable period, discontinue use and institute appropriate therapy.

Stevens-Johnson syndrome, toxic epidermal necrolysis and anaphylactic reaction/shock have been reported in patients receiving EXOCIN®.

Corneal precipitates, and corneal perforation in patients with pre-existing corneal epithelial defect or corneal ulcer, have been reported during treatment with EXOCIN®.

Long-term, high-dose use of fluoroquinolones in experimental animals has caused lenticular opacities. However, this effect has not been reported in human patients.

EXOCIN® contains the preservative benzalkonium chloride, which may cause eye irritation.

As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmic preparations cannot be excluded, regular ophthalmological examination is required.

Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.

The use of EXOCIN® while wearing soft contact lenses is not recommended. Benzalkonium chloride may be absorbed by soft contact lenses and discolour them. Contact lenses should be removed prior to installation and may be reinserted 15 minutes following administration.

Geriatric use
No comparative data are available with topical dosing in the elderly versus other age groups.

Paediatric use
Safety and effectiveness in infants below the age of one year have not been established.

The use of EXOCIN® eye drops in neonates with ophthalmia neonatorum caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* is not recommended as it has not been evaluated in such patients. Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition, e.g. systemic treatment in cases caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae.*

Ofloxacin have been shown to cause arthropathy in immature animals after oral administration; however, topical ocular administration of EXOCIN® to immature animals has not shown any arthropathy (see ‘CONTRAINDICATIONS’).

Effects on the ability to drive and use machines

Transient blurring of vision may occur on instillation of eye drops. Do not drive or operate hazardous machinery unless vision is clear.

INTERACTIONS

It has been shown that the systemic administration of some quinolones inhibits the metabolic clearance of caffeine and theophylline. 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 central nervous system toxicity with systemic dosing of fluoroquinolones when used concomitantly with systemic non-steroidal anti-inflammatory drugs (NSAIDs), this has not been reported with the concomitant systemic use of NSAIDs and ofloxacin.

No interaction studies with EXOCIN® have been performed.

PREGNANCY AND LACTATION

Pregnancy

Since systemic quinolones have been shown to cause arthropathy in immature animals, it is recommended that EXOCIN® not be used in pregnant women (see 'CONTRAINDICATIONS').

Lactation

Ofloxacin and other quinolones are excreted in breast milk, therefore there is a potential for harm to nursing infants. EXOCIN® is not recommended for breastfeeding women and temporary discontinuation of breastfeeding should be considered (see 'CONTRAINDICATIONS').

DOSAGE AND DIRECTIONS FOR USE

The recommended dosage for the treatment of bacterial conjunctivitis is:

One drop every two to four hours for the first two days, then four times daily in the affected eye(s).

Treatment should not exceed ten days.

The recommended dosage regimen for the treatment of bacterial corneal ulcer is:

Days 1 and 2: Instil one to two drops into the affected eye every 30 minutes, while awake. Awaken at approximately four and six hours after retiring and instil one to two drops.

Days 3 through 7 to 9: Instil one or two drops hourly, while awake.

Days 7 to 9 through treatment completion: Instil one to two drops, four times daily.

SIDE EFFECTS

General

Since a small amount of EXOCIN® is systemically absorbed after topical administration, adverse events reported with systemic use could possibly occur.

Nervous system disorders

Frequency unknown: Dizziness

Eye disorders

Frequent: Eye irritation, ocular discomfort

Frequency unknown: Keratitis, conjunctivitis, vision blurred, photophobia, eye oedema, foreign body sensation in eyes, lacrimation increased, dry eye, eye pain, eye pruritus, eyelids pruritus, ocular hyperaemia, periorbital oedema (including eyelid oedema)

Gastrointestinal disorders

Nausea

Skin and subcutaneous tissue disorders

Frequency unknown: Stevens-Johnson syndrome

Immune system disorders

Frequency unknown: Hypersensitivity reactions, anaphylactic reactions (such as angioedema, dyspnea, anaphylactic shock, oropharyngeal swelling and tongue swollen) and allergic dermatitis

General disorders and administrative site conditions

Frequency unknown: Facial oedema

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

In the event of accidental ingestion of 10 ml of EXOCIN®, 30 mg of ofloxacin would be ingested. This amount does not appear to be clinically significant in terms of overdosage. However, there would be an increased potential for systemic reactions (see 'WARNINGS AND SPECIAL PRECAUTIONS').

In the event of a topical overdosage, flush the eye with a topical ocular irrigant.

Treatment is symptomatic and supportive.

IDENTIFICATION

EXOCIN® is a clear, pale to light yellow-green solution practically free from particulate matter.

PRESENTATION

EXOCIN® is supplied in sterile dropper bottles containing 5 ml solution.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Do not use more than 30 days after opening.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

Z/15.1/347

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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