SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

EXOCIN 3mg/ml Eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One millilitre contains 3.0 mg ofloxacin (0.3% w/v).

Excipient with known effect:
One ml of solution contains 0.05mg of benzalkonium chloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.

Clear, pale to light yellow-green solution, practically free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Exocin is indicated for the topical treatment of external ocular infections (such as conjunctivitis and keratoconjunctivitis) in adults and children caused by ofloxacin - sensitive organisms. Safety and efficacy in the treatment of ophthalmia neonatorum has not been established.

4.2 Posology and method of administration

Topical ocular instillation.

For all ages: one to two drops in the affected eye(s) every two to four hours for the first two days and then four times daily. The length of treatment should not exceed ten days.

4.3 Contraindications

EXOCIN® is contra-indicated in individuals who have shown hypersensitivity to ofloxacin, any of its excipients or any other quinolones.

4.4 Special warnings and precautions for use

EXOCIN® is not for injection.

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

Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions, some following the first dose, have been reported in patients receiving systemic quinolones, including 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 drug. Use EXOCIN® with caution in patients who have exhibited sensitivities to other quinolones antibacterial agents.

When using EXOCIN® the risk of rhinopharyngeal passage which can contribute to the occurrence and the diffusion of bacterial resistance should be considered. As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms.

If worsening infection occurs, or if clinical improvement is not noted within a reasonable period, discontinue use and institute alternative therapy.

Stevens-Johnson syndrome has been reported in patients receiving topical ophthalmic ofloxacin, however, a causal relationship has not been established.

Use EXOCIN® with caution in patients who have exhibited sensitivities to other quinolone antibacterial agents.

Data are very limited to establish efficacy and safety of EXOCIN® eye drops 0.3% in the treatment of conjunctivitis in neonates.

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.

Use in elderly: No comparative data are available with topical dosing in elderly versus other age groups.

Clinical and non-clinical publications have reported the occurrence of corneal perforation in patients with pre-existing corneal epithelial defect or corneal ulcer, when treated with topical fluoroquinolone antibiotics. However, significant confounding factors were involved in many of these reports, including advanced age, presence of large ulcers, concomitant ocular conditions (e.g. severe dry eye), systemic inflammatory diseases (e.g. rheumatoid arthritis), and concomitant use of ocular steroids or non-steroidal anti-inflammatory drugs. Nevertheless, it is necessary to advise caution regarding the risk of corneal perforation when using product to treat patients with corneal epithelial defects or corneal ulcers.

Corneal precipitates have been reported during treatment with topical ophthalmic ofloxacin. However, a causal relationship has not been established.

Long-term, high-dose use of other fluoroquinolones in experimental animals has caused lenticular opacities. However, this effect has not been reported in human patients, nor has it been noted following topical ophthalmic treatment with ofloxacin for up to six months in animal studies including studies in monkeys.

EXOCIN® contains the preservative benzalkonium chloride which may cause ocular irritation and discolour soft contact lenses.

Sun or UV-exposition should be avoided during use of ofloxacin due to the potential for photosensitivity.

Use of contact lenses is not recommended in patients receiving treatment for an eye infection.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

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

4.6 Fertility, Pregnancy and lactation

Pregnancy
There have been no adequate and well-controlled studies performed in pregnant women. Since systemic quinolones have been shown to cause arthropathy in immature animals, it is recommended that EXOCIN® not be used in pregnant women.

Breastfeeding
Because ofloxacin and other quinolones taken systemically are excreted in breast milk, and there is potential for harm to nursing infants, a decision should be made whether to temporarily discontinue nursing or not to administer the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

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

4.8 Undesirable effects

General
Serious reactions after use of systemic ofloxacin are rare and most symptoms are reversible. Since a small amount of ofloxacin is systemically absorbed

after topical administration, side-effects reported with systemic use could possibly occur.

Frequency categories: 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) and not known (cannot be estimated from the available data):

Immune System Disorders:
Very rare: Hypersensitivity* (including angioedema, dyspnea, anaphylactic reaction/shock, oropharyngeal swelling and tongue swollen).
* Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions, some following the first dose, have been reported in patients receiving systemic quinolones, including ofloxacin. See section 4.4.

Nervous System Disorders
Not known: Dizziness

Eye Disorders
Common: Eye irritation; Ocular discomfort
Not known: Keratitis; Conjunctivitis; Vision blurred; Photophobia; Eye oedema; Foreign body sensation in eyes; Lacrimation increased; Dry eye; Eye pain; Ocular hyperaemia; Hypersensitivity (including Eye pruritus and Eyelid pruritus).

Gastrointestinal Disorders
Not known: Nausea

Skin and Subcutaneous Tissue Disorders
Not Known: Periorbital oedema, Facial oedema

4.9 Overdose

No case of overdose has been reported.
In the event of a topical overdosage, flush the eye with water.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, anti-infectives, fluoroquinolones
ATC code: S01AE01.

Ofloxacin is a synthetic fluorinated 4-quinolone antibacterial agent with activity against a broad spectrum of Gram negative and to lesser degree Gram positive organisms.

Ofloxacin has been shown to be active against most strains of the following organisms both in vitro and clinically in ophthalmic infections. Clinical trial evidence of the

efficacy of EXOCIN® against S. pneumoniae was based on a limited number of isolates.

Gram-negative bacteria: Acinetobacter calcoaceticus var. anitratum, and A. calcoaceticus var. iwoffi; Enterobacter Sp. including E. cloacae; Haemophilis Sp, including H. influenza and H. aegyptius; Klebsiella Sp., including K. Pneumoniae; Moraxella Sp., Morganella morganii; Proteus Sp., including P. Mirabilis; Pseudomonas Sp.; including P. Aeruginosa, P. cepacia, and P. fluoroscens; and Serratia Sp., including S. marcescens.

Gram-positive bacteria: Bacillus Sp.; Corynebacterium Sp.; Micrococcus Sp.; Staphylococcus Sp., including S. aureus and S. epidermidis; Streptococcus Sp., including S. Pneumoniae (see above), S. viridans and Beta-haemolytic.

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

Ofloxacin is not subject to degradation by beta-lactamase enzymes nor is it modified by enzymes such as aminoglycoside adenylases or phosphorylases, or chloramphenicol acetyltransferase.

5.2 Pharmacokinetic properties

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

Maximum serum ofloxacin concentrations after ten days of topical dosing were about 1000 times lower than those reported after standard oral doses of ofloxacin, and no systemic side-effects attributable to topical ofloxacin were observed.

5.3 Preclinical safety data

There are no toxicological safety issues with this product in man as the level of systemic absorption from topical ocular administration of ofloxacin is minimal.

Animal studies in the dog have found cases of arthropathy in weight bearing joints of juvenile animals after high oral doses of certain quinolones.

However, these findings have not been seen in clinical studies and their relevance to man is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Sodium chloride
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Purified water (EP)

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years unopened.
Discard 28 days after first opening.

6.4 Special precautions for storage

Do not store above 25^{o}C.

6.5 Nature and contents of container

A bottle and an applicator tip of low density polyethylene (LDPE) and medium or high impact polystyrene cap.
The bottle contains 5 ml or 10 ml of suspension.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

There is no special requirement for disposal.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

AbbVie Ltd.
Maidenhead
SL6 4UB
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 41042/0064

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th October 1992
Date of last renewal: 8th November 2004

10 DATE OF REVISION OF THE TEXT

01/04/2022