IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0290/069/001
Case No: 2069252

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Alcon Laboratories (UK) Ltd

Pentagon Park, **Boundary Way**, **Hemel Hempstead**, **Hertfordshire HP2 7UD**, **England**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Ciloxan 0.3% w/v Eye Drops Solution

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **24/02/2010** until **12/11/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ciloxan 0.3% w/v Eye Drops Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

3 PHARMACEUTICAL FORM

Eye drops, solution

A clear, colourless to pale yellow sterile solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adults, newborn infants (0-27 days), infants and toddlers (28 days to 23 months), children (2-11 years) and adolescents (12 – 16 years)

CILOXAN is indicated for the management of corneal ulcers, conjunctivitis and blepharitis due to microorganisms resistant to other antibiotics.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

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:

CILOXAN 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.

Bacterial Conjunctivitis/Blepharitis:

For the first 2 days intill 1 or 2 drops into the conjunctival sac(s) of the infected eye(s) every 2 hours while awake. Then 1 or 2 drops every 4 hours while awake until the bacterial infection is resolved.

The safety and efficacy of CILOXAN in children has not been established.

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

Ciloxan should be administered under the supervision of a specialist opthalmology service, having the facilities for regular monitoring of clinical and microbiological effects during and after administration.

Prolonged use of an anti-infective including ciprofloxacin, may lead to superinfection with organisms, including fungi, resistant to the anti-infective.

Although the extent of systemic absorption is too low to induce systemic toxicity, it is sufficient to precipitate serious allergic reactions, in particular anaphylaxis and cardiovascular collapse. However such reactions were not observed in opthalmaic ciprofloxacin clinical trials.

Likewise Ciloxan should be suspended immediately at the first appearance of a skin rash or any other sign of hypersensitivity reaction and medical advice should be sought.

This product contains benzalkonium chloride, a preservative that may cause eye irritation and is known to discolour soft contact lenses. Contact lenses should not be worn during treatment with Ciloxan.

4.5 Interaction with other medicinal products and other forms of interaction

Concentrations of systemically circulating ciprofloxacin are insufficient to be associated with interactions with systemically administered drugs. However no information is available concerning interactions with agents locally instilled in the conjunctival sac.

If supplementary eye preparations are to be used, one should wait about 15 minutes between the two applications.

4.6 Pregnancy and lactation

For CILOXAN 0.3% Eye Drops no clinical data from well-controlled studies in pregnant women are available.

Animals studies do not indicate direct or indirect harmful effects with respect to fertility and embryonic/foetal development. Studies in rabbits have shown an increased risk of abortion due to maternal weight loss. The relevance of these data for humans is unknown.

CILOXAN 0.3% Eye Ointment should not be used during pregnancy unless clearly necessary and only if the potential benefit justifies the potential risk to the foetus.

It is not known whether topically applied Ciprofloxacin is excreted in human milk. It crosses the placenta and is excreted in breast milk and amniotic fluid in animal studies.

Caution should be exercised when CILOXAN 0.3% Eye Drops is administered to a nursing mother.

As with other quinolones, ciprofloxacin has been shown to cause arthropathy in immature animals. There is no evidence that the ophthalmic dosage form of ciprofloxacin has any effect on weight bearing joints.

Plasma levels of drug are very low after use of ophthalmic drops. Nevertheless the product should only be used in pregnancy or lactation if considered essential by the physician.

4.7 Effects on ability to drive and use machines

Temporarily blurred vision or other visual disturbances may effect the ability to drive or use machines. If blurred vision or visual disturbances occur, the patient must wait until the vision is clear before driving or using machinery.

4.8 Undesirable effects

Immune System Disorders
Very rare (< 0.01%): hypersensitivity (systemic). *(See Section 4.4)*

Nervous System Disorders
Common (≥ 1% < 10%): dysgeusia.

Eye Disorders
Common (≥ 1% < 10%): eye irritation, ocular discomfort, eye pruritus, foreign body sensation in eyes, eyelid margin crusting, ocular hyperaemia.

Uncommon (≥ 0.1% < 1%): keratopathy, keratitis, eye allergy, eyelid oedema, lacrimation increased, photophobia, visual acuity reduced.

Investigations
Uncommon (≥ 0.1% <1%): corneal staining.

Injury, Poisoning and Procedural Complications
Uncommon (≥ 0.1% < 1%): medication residue.

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

In isolated cases blurred vision, decreased visual acuity and medication residue have been observed with ophthalmic ciprofloxacin.

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.

4.9 Overdose

A topical overdose of CILOXAN is unlikely to be associated with toxicity. A topical overdose of CILOXAN may be flushed from the eyes with lukewarm tap water. Accidental ingestion of CILOXAN is also not likely to be associated with toxicity. Treatment of a suspected ingestion is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:Antiinfectives; Other Antiinfectives
ATC Code: SO1A X13

Ciprofloxacin has cidal and inhibitory activities against bacteria which result 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 any longer which causes a breakdown of the bacterial metabolism.

5.2 Pharmacokinetic properties

After topical ocular administration, ciprofloxacin is absorbed systemically. Plasma levels in volunteers ranged from nonquantifiable to 4.7ng/mL (some 450-fold less than levels observed following sample 250mg oral administration.

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

5.3 Preclinical safety data

Ciprofloxacin and other quinolones have been shown to cause arthropathy in immature animals of most species tested following oral administration. The degree of cartilage involvement was found to be dependent on age, species and dosage. With 30 mg/kg ciprofloxacin the effect on the joint was minimal.

A one month topical ocular study with ciprofloxacin 3mg/ml eye drops, solution in immature beagle dogs did not demonstrate any articular lesions. Likewise there is no evidence that the ophthalmic dosage form has any effect on the weight bearing joints.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Disodium edetate
Mannitol
Acetic acid
Sodium acetate
Hydrochloric acid / Sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Incompatible with alkaline solutions.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.
Discard any remaining contents one month after first opening.

6.5 Nature and contents of container

Low density polyethylene dropper container containing 5 ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Limited
Pentagon Park
Boundary Way
Hemel Hempstead
Herts HP2 7UD
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0290/069/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 13 November 1995

Date of last renewal: 13 November 2005

10 DATE OF REVISION OF THE TEXT

February 2010