PACKAGE INSERT FOR XINOCT ® OPHTHALMIC SOLUTION

SCHEDULING STATUS **S4**

PROPRIETARY NAME AND DOSAGE FORM

Xinoct® Ophthalmic Solution

COMPOSITION

Each ml of XINOCT Ophthalmic Solution contains: ciprofloxacin hydrochloride equivalent to 3 mg ciprofloxacin.

Preservative: 0,006 % *m/v* benzalkonium chloride.

The other ingredients are edetate disodium, mannitol, sodium acetate anhydrous and water for injection.

PHARMACOLOGICAL CLASSIFICATION

A. 15.1 Ophthalmic preparations with antibiotics and/or sulphonamides.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Ciprofloxacin is a broad spectrum, water soluble fluoroquinolone antibacterial. It is bactericidal and acts by inhibiting DNA gyrase, an enzyme required by bacterium for the synthesis of DNA.

As a result, the vital information from the bacterial chromosome can no longer be transcribed resulting in a breakdown in the bacterial metabolism.

Resistant organisms:

Resistance to ciprofloxacin has usually been chromosomally-mediated, although plasma-mediated resistance has recently been noted.

Most anaerobic bacteria, including *Bacteroides fragilis* and *Clostridium difficile* are resistant to ciprofloxacin.

The following organisms have acquired resistance to ciprofloxacin: methicillin-resistant *Staphylococcus aureus* (MRSA), *P. aeruginosa, E. coli, Klebsiella pneumonia, C. jejuni, N. gonorrhoea,* and *Str. pneumonia.*

Pharmacokinetic properties:

Following topical ocular administration, ciprofloxacin is absorbed systemically. The mean plasma concentration was less than 2,5 ng/ml and the maximum reported plasma concentration of ciprofloxacin was less than 5 ng/ml (some 450-fold less than levels observed following simple 250 mg oral administration).

INDICATIONS

XINOCT Ophthalmic Solution is indicated for the treatment of corneal ulceration and conjunctivitis caused by susceptible strains of bacteria.

Appropriate monitoring of bacterial response to topical antibacterial therapy should accompany the use of XINOCT Ophthalmic Solution.

CONTRAINDICATIONS

- Hypersensitivity to ciprofloxacin or any of the ingredients in this medication.
- Hypersensitivity to other quinolones may also contraindicate the use of ciprofloxacin.

WARNINGS AND SPECIAL PRECAUTIONS

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

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been observed in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, facial or pharyngeal facial oedema, dyspnoea, itching and urticaria. Only a few patients had a history of hypersensitivity reactions. As clinically indicated, serious anaphylactic reactions require immediate emergency treatment with epinephrine (adrenalin) and other resuscitation measures, including oxygen, intravenous antihistamines, intravenous fluids, corticosteroids, pressor amines and airway management.

When using XINOCT Ophthalmic Solution the risk of rhinopharyngeal passage should be taken into account which can contribute to the occurrence and diffusion of bacterial resistance.

Contact lenses should be removed before XINOCT Ophthalmic Solution is instilled.

Tendon inflammation and rupture may occur with systemic ciprofloxacin, particularly in elderly patients and those treated concurrently with corticosteroids. Therefore, treatment with XINOCT Ophthalmic Solution should be discontinued at the first sign of tendon inflammation.

Prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, appropriate measures should be initiated. Whenever clinical judgement dictates, the patient should be examined with the aid of magnification, such as biomicroscopy and slit-lamp and where appropriate, fluorescein staining.

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 ophthalmological 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.

White precipitate and ocular discomfort (stinging and burning) may occur upon administration. In patients with corneal ulcer or frequent administration of ciprofloxacin, white precipitates have been reported, which

resolved spontaneously with continued application. The precipitate does not adversely affect the clinical course of the ulcer or the recovery process, nor does it preclude continued use of XINOCT Ophthalmic Solution.

INTERACTIONS

The systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine and enhance the effect of warfarin and its derivatives. Transient increases in serum creatinine have been observed in patients receiving ciclosporin concomitantly.

PREGNANCY AND LACTATION

Safety in pregnant women and breastfeeding mothers has not been established.

DOSAGE AND DIRECTIONS FOR USE

Incorrect handling of XINOCT Ophthalmic Solution can result in bacterial contamination of the solution and subsequent ocular infections. Allowing the tip of the dispensing container to come in contact with the eye or surrounding areas should therefore be avoided.

The recommended dosage regimens for adults and children over the age of two years are as follows:

- **Corneal ulcers or abscesses:**
  On the first day, instil two drops into the affected eye every 15 minutes for the first six hours and then two drops into the affected eye every 30 minutes for the remainder of the day.
  On the second day, instil two drops into the affected eye hourly.
  On the third through fourteenth day instil two drops into the affected eye every four hours.
  If the patient needs to be treated longer than 14 days, the dosing regimen is at the discretion of the medical practitioner.

- **Bacterial conjunctivitis:**
  Instil one or two drops into the conjunctival sac(s) every two hours while awake for two days.
  Thereafter instil one or two drops into the conjunctival sac(s) every four hours while awake until the bacterial infection is resolved.

SIDE EFFECTS

Infections and infestations:

Less frequent: Hordeolum, rhinitis.

Immune system disorders:

Less frequent: Hypersensitivity.

Nervous system disorders:

Frequent: Dysgeusia.

Less frequent: Headache, dizziness.

Eye disorders:
Frequent: Corneal deposits, ocular discomfort, ocular hyperaemia.
Less frequent: Itching, foreign body sensation, lid margin crusting, crystals/scales, conjunctival hyperaemia, conjunctival oedema, corneal staining, keratopathy/keratitis, allergic reactions, lid oedema, tearing, photophobia, corneal infiltrates and decreased visual acuity, erythema of eyelid, blurred vision, eye pain, dry eye, eye swelling, eye pruritus, increased eye discharge, eyelid exfoliation, conjunctivitis, diplopia, eye irritation, eye inflammation, eye hypoaesthesia.

Gastro-intestinal disorders:
Less frequent: Nausea, taste perversion (metallic taste), diarrhoea, abdominal pain.

Skin and subcutaneous tissue disorders:
Less frequent: Dermatitis.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

(See "Side Effects" and "Warnings and Special Precautions")

A topical ocular overdose may be flushed from the eye(s) with warm tap water. Treatment should be symptomatic and supportive.

IDENTIFICATION

XINOCT Ophthalmic Solution is a clear, colourless solution.

PRESENTATION

5 ml translucent, low density polyethylene vial with white to off-white high impact polystyrene spike cap containing 5 ml sterile XINOCT Ophthalmic Solution packed in a carton.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Protect from light.
Do not refrigerate or freeze.
Do not use more than 30 days after opening.
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

47/15.1/0959

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

Actor Pharma (Pty) Ltd[1]
Unit 7, Royal Palm Business Estate

646 Washington Street, Halfway House
Midrand, 1685
Gauteng, South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT

03 September 2015

® - XINOCT is a registered trademark of Actor Pharma (Pty) Ltd.

[1] Company Registration number: 2008/008787/07

XIN/PI/01/11.2017