**S4**

**SCHEDULING STATUS**

**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**
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**DATE OF PUBLICATION OF THE PACKAGE INSERT**
03 September 2015

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1 Company Registration number: 2008/008787/07

**XIN/PI/01/11.2017**

**SKEDULERINGSTATUS S4**

**EIENDOMSNAAM EN DOSEERVORM**

**Xinoct®** **Oftalmiese Oplossing**

**SAMESTELLING**

Elke ml XINOCT Oftalmiese Oplossing bevat siprofloksasienhidrochloried gelykstaande aan 3 mg siprofloksasien.

Bewaarmiddel: 0,006 % *m/v* bensalkoniumchloried.

Die ander bestanddele is dinatriumedetaat, mannitol, natriumsitraat (anhidries) en water vir inspuiting.

**FARMAKOLOGIESE KLASSIFIKASIE**

A. 15.1 Oftalmiese preparate met antibiotika en/of sulfoonamiede.

**FARMAKOLOGIESE WERKING**

**Farmakodinamiese eienskappe:**

Siprofloksasien is ’n breëspektrum, wateroplosbare antibakteriese fluorokinolone. Dit is bakterisidies en werk deur DNA-girase te rem, ’n ensiem wat bakterie vir die sintese van DNA nodig het.

As gevolg hiervan kan die belangrike inligting van die bakteriële chromosoom nie meer getranskribeer word nie wat tot ’n ineenstorting van die bakteriële metabolisme lei.

*Weerstandige organismes:*

Weerstand teen siprofloksasien word gewoonlik deur chromosome bemiddel, hoewel plasmabemiddelde weerstand onlangs opgemerk is.

Die meeste anaërobiese bakterieë, waaronder *Bacteroides fragilis* en *Clostridium difficile* is bestand teen siprofloksasien.

Die volgende organismes het weerstand teen siprofloksasien opgebou: metisillienweerstandige *Staphylococcus aureus* (MRSA), *P. aeruginosa, E. coli, Klebsiella pneumoniae, C. jejuni, N. gonorree* en *Str. pneumoniae*.

**Farmakokinetiese eienskappe:**

Na toediening in die oog word siprofloksasien sistemies geabsorbeer. Die gemiddelde plasmakonsentrasie was minder as 2,5 ng/ml en die maksimum aangemelde plasmakonsentrasie van siprofloksasien was minder as 5 ng/ml (450 keer minder as vlakke waargeneem na eenvoudige toediening van 250 mg oraal).

**INDIKASIES**

XINOCT Oftalmiese Oplossing is aangedui vir die behandeling van korneale ulserasie en konjunktivitis veroorsaak deur vatbare stamme van bakterieë.

Toepaslike monitering van bakteriële reaksie op topikale antibakteriese middels moet tydens die gebruik van XINOCT Oftalmiese Oplossing gedoen word.

**KONTRA-INDIKASIES**

* Hipersensitiwiteit teenoor siprofloksasien of enige van die bestanddele in hierdie medikasie.
* Hipersensitiwiteit teenoor ander kinolone kan ook ’n kontra-indikasie vir die gebruik van siprofloksasien wees.

**WAARSKUWINGS EN SPESIALE VOORSORGMAATREëLS**

XINOCT Oftalmiese Oplossing moet gestaak word met die eerste tekens van ‘n veluitslag of enige ander teken van hipersensitiwiteit.

Ernstige en soms dodelike hipersensitiwiteitsreaksies (anafilakse) is gesien in pasiënte wat sistemiese kinoliene ontvang het. Sommige reaksies het met kardiovaskulêre ineenstorting, verlies van bewussyn, tinteling, edeem van die gesig of keel, dispnee, jeuk en urtikarie gepaardgegaan. Slegs ’n paar pasiënte het ’n geskiedenis van hipersensitiwiteitsreaksies. Soos klinies aangedui, kan onmiddellike noodbehandeling met adrenalien (epinefrien) en ander maatreëls vir resussitasie, waaronder suurstof, binneaarse antihistamiene, binneaarse vloeistowwe, kortikosteroïede, pressoramiene en lugwegbestuur vir ernstige anafilaktiese reaksies nodig wees.

Wanneer XINOCT Oftalmiese Oplossing gebruik word, moet die risiko van rinofaringeale deurgang in ag geneem word wat kan bydra tot die voorkoms en verspreiding van bakteriële weerstand.

Kontaklense moet verwyder word voordat XINOCT Oftalmiese Oplossing ingedrup word.

Inflammasie en ruptuur van die tendons kan tydens behandeling met sistemiese siprofloksasien voorkom en veral in bejaarde pasiënte en in diegene wat terselfdertyd met kortikosteroïede behandel word. Daarom moet behandeling met XINOCT Oftalmiese Oplossing met die eerste tekens van tendoninflammasie gestaak word.

Langdurige gebruik kan oorgroei van nie-vatbare organismes, waaronder fungi, veroorsaak. Indien superinfeksie voorkom, moet geskikte maatreëls ingestel word. Wanneer kliniese oordeel dit noodsaak, moet die pasiënt met behulp van vergroting, soos biomikroskopie en ’n spleetlamp, en waar toepaslik, fluoressienkleuring, ondersoek word.

Omdat die moontlikheid vir nadelige effekte op die deurlaatbaarheid van die kornea en die gevaar van versteuring van die epiteel van die kornea met langdurige of herhaaldelike gebruik van oftalmiese preparate wat bensalkoniumchloried bevat nie uitgesluit kan word nie, is gereelde oftalmiese ondersoeke nodig. Wees versigtig met die gebruik van topikale medikasie met bensalkoniumchloried oor ŉ lang periode vir pasiënte met uitgesproke siekte van die oogoppervlak.

Wit neerslag en okulêre ongemak (steek- en brandgevoel) kan na toediening voorkom. ’n Wit neerslag is aangemeld in pasiënte met korneale ulkus of met gereelde toediening van siprofloksasien, wat na voortgesette toediening spontaan opgeklaar het. Die neerslag het nie die kliniese verloop van die ulkus of die herstelproses nadelig beïnvloed nie, en ook nie voortgesette gebruik van XINOCT Oftalmiese Oplossing verhinder nie.

**INTERAKSIES**

Dit is getoon dat die sistemiese toediening van sekere kinolone plasmakonsentrasies van teofillien verhoog, inmeng met die metabolisme van kaffeïen en die effek van warfarin en sy derivate versterk. Verbygaande stygings in kreatinienvlakke in die serum is waargeneem in pasiënte wat siklosporien saam kry.

**SWANGERSKAP EN BORSVOEDING**

Die veiligheid vir swanger en borsvoedende moeders is nie bepaal nie.

**DOSIS EN GEBRUIKSAANWYSINGS**

Verkeerde hantering van XINOCT Oftalmiese Oplossing kan tot bakteriële besmetting van die oplossing en gevolglike ooginfeksies lei. Verhoed dus dat die punt van die botteltjie in kontak met die oog of omliggende area kom.

Die aanbevole doserings skedule vir volwassenes en kinders ouer as twee jaar is soos volg:

* **Korneale sere of absesse:**

Drup op die eerste dag vir die eerste ses uur elke 15 minute twee druppels in die geaffekteerde oog en dan twee druppels in die geaffekteerde oog elke 30 minute vir die res van die dag.

Drup op die tweede dag elke uur twee druppels in die geaffekteerde oog.

Drup op die derde tot die veertiende dag elke vier uur twee druppels in die geaffekteerde oog.

As die pasiënt behandeling vir langer as 14 dae nodig het, is die dosering volgens die diskresie van die geneesheer.

* **Bakteriële konjunktivitis:**

Drup vir twee dae elke twee uur terwyl wakker een of twee druppels in die konjunktivale sakkie(s).

Drup daarna elke vier uur terwyl wakker een of twee druppels in die konjunktivale sakkie(s) tot die bakteriële infeksie opgeklaar het.

**NEWE-EFFEKTE**

**Infeksies en infestasies:**

*Minder dikwels:* Hordeolum, rinitis.

**Versteurings van die immuunstelsel:**

*Minder dikwels:* Hipersensitiwiteit.

**Versteurings van die senustelsel:**

*Dikwels:* Smaakversteuring.

*Minder dikwels:* Hoofpyn, duiseligheid.

**Versteurings van die oë:**

*Dikwels:* Korneale neerslag, okulêre ongemak, okulêre hiperemie.

*Minder dikwels:* Jeuk, sensasie van vreemde voorwerp, korsvorming op die rand van die ooglede, kristalle/skubbe, konjunktivale hiperemie, konjunktivale edeem, korneale vlekke, keratopatie/keratitis, allergiese reaksies, ooglidedeem, trane, fotofobie, korneale infiltrate en swakker gesigskerpte, eriteem van ooglid, versteurde visie, oogpyn, droë oë, oogswelling, oogpruritus, meer afskeiding uit die oog, afskilfering op ooglede, konjunktivitis, diplopie, oogirritasie, ooginflammasie, ooghipestesie.

**Gastro-intestinale versteurings:**

*Minder dikwels:* Naarheid, smaakperversie (metaalsmaak), diarree, abdominale pyn.

**Versteurings van vel en subkutane weefsel:**

*Minder dikwels:* Dermatitis.

**BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN**

**(Kyk “Newe-effekte” en “Spesiale voorsorgmaatreëls”).**

ŉ Lokale oordosis in die oë kan met warm kraanwater uit die oog(oë) gespoel word. Behandeling is simptomaties en ondersteunend.

**IDENTIFIKASIE**

XINOCT Oftalmiese Oplossing is ’n helder, kleurlose oplossing.

**AANBIEDING**

Flessie van 5 ml van deursigtige, lae-digtheid poliëtileen met ’n wit tot naaswit doppie van hoë impak polistireen met ’n pen in, met 5 ml steriele XINOCT Oftalmiese Oplossing verpak in ’n karton.

**BEWARINGSINSTRUKSIES**

Bêre by of onder 25 °C. Beskerm teen lig.

Moenie verkoel of vries nie.

Moenie vir langer as 30 dae nadat dit oopgemaak is, gebruik nie.

HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS.

**REGISTRASIENOMMER**

47/15.1/0959

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**DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET**

03 September 2015

® - XINOCT is ’n geregistreerde handelsmerk van Actor Pharma (Edms) Bpk.

1 Maatskappyregistrasienommer: 2008/008787/07

**XIN/PI/01/11.2017**