PROFFESIONAL INFORMATION

FOR OCTIN (EYE DROPS)

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

OCTIN (Ophthalmic drops)

COMPOSITION:

Each 5 mℓ contains 15 mg ofloxacin (0,3 % *w/v*).

Inactive ingredient is disodium edetate.

Preservative: Benzalkonium chloride 0,01 % *w/v*

Contains no sugar

PHARMACOLOGICAL CLASSIFICATION:

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

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Ofloxacin is a fluorinated 4-quinolone antibacterial medicine and its anti-bactericidal action results from interference with the enzyme, DNA gyrase, which is needed for the synthesis of bacterial DNA. Vital information needed from the

bacterial chromosomes cannot be transcribed, causing the breakdown of bacterial metabolism. Replicating and non-replicating stages of bacterial growth are affected by the bactericidal effect of ofloxacin and a broad spectrum of antibacterial activity is demonstrated against Gram-negative, and to a lesser extent, Gram-positive organisms. Studies have shown that 90 % of most susceptible bacteria are eliminated within 4 hours and an inhibitory effect is maintained on the cell growth for 6 – 8 hours after drug removal.

Cross-resistance has been observed between ofloxacin and other fluoroquinolones. Resistance has increased, especially in *Pseudomonas* and staphylococci. Increasing fluoroquinolone resistance is also observed in *C. jejuni, Salmonella, N. gonorrhoeae and S. pneumoniae*.

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.

Pharmacokinetics (for ocular administration):

Low serum levels of ofloxacin were detected after ocular administration.

Ofloxacin is eliminated mainly by the kidneys.

INDICATIONS:

OCTIN is indicated for the treatment of conjunctivitis and corneal ulcers caused by susceptible organisms. Safety and efficacy in the treatment of ophthalmia neonatorum has not been established.

CONTRAINDICATIONS:

OCTIN is contraindicated:

- In patients with hypersensitivity to ofloxacin, fluoroquinolones or their derivatives, or any of the components of **OCTIN**.
- While wearing soft contact lenses.
- During pregnancy and lactation, since systemic quinolones have been shown to cause arthropathy in immature animals (see **"PREGNANCY AND LACTATION"** and **"WARNINGS AND SPECIAL PRECAUTIONS"**).
- In infants under one year, since safety and efficacy have not been established.
- Concomitant use of fluoroquinolones with ACE inhibitors/Renin-Angiotensin blockers is contraindicated in patients with moderate to severe renal impairment.
- In patients with confirmed mitral valve and / aortic valve regurgitation unless no safer appropriate alternative antibiotic is available, has failed or is not well tolerated.

WARNINGS AND SPECIAL PRECAUTIONS:

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 (see **"SIDE EFFECTS"**). **OCTIN** should be used with caution in patients with known hypersensitivity to other quinolone antibacterial medicine. Should hypersensitivity reactions develop, therapy with **OCTIN** should be discontinued. Mild hypersensitivity reactions may be treated with antihistamines and, if necessary, glucocorticoids.

Stevens-Johnson syndrome which progressed to toxic epidermal necrolysis has been reported. If an allergic reaction to **OCTIN** occurs, discontinue **OCTIN**.

Patients should be informed that if the condition does not improve within 7 days they should consult a doctor.

Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Super-infection may occur with prolonged use. If clinical improvement does not occur within a reasonable period, it is recommended that treatment with **OCTIN** be discontinued and appropriate therapy instituted.

When using **OCTIN** the risk of rhinopharyngeal passage, which can contribute to the occurrence and the diffusion of bacterial resistance, should be considered.

Caution should be taken when using **OCTIN**, in patients with known risk factors for prolongation of the QT interval, such as:

- Congenital long QT syndrome.
- Concomitant use of medicines that are known to prolong the QT interval (e.g. Class IA and III anti-dysrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
- Uncorrected electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia).
- Cardiac disease (e.g. heart failure, myocardial infarction, bradycardia).

Elderly patients and women may be more sensitive to QTc-prolonging medicines. Therefore, caution should be taken when using fluoroquinolones, including **OCTIN**, in these populations.

Disturbances in blood glucose, including both hyperglycaemia and hypoglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic medicine or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended (see **"SIDE EFFECTS"**).

Should severe and persistent diarrhoea occur during or after therapy with **OCTIN**, a medical practitioner should be informed, since this may indicate a serious intestinal disorder (pseudomembranous colitis), requiring immediate medical treatment. Treatment with **OCTIN** should be discontinued immediately.

Use in children:

Safety and efficacy has not been established in infants under one year of age (see **"CONTRAINDICATIONS"**). The use of **OCTIN** eye drops is not recommended in the treatment of neonates with ophthalmia neonatorum caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, as it has not been evaluated in such patients. Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition such as systemic treatment in cases caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

The systemic administration of quinolones, including ofloxacin, has led to lesions or erosions of the cartilage in weight bearing joints and other signs of arthropathy in immature animals of various species. Ofloxacin, administered systemically at 10 mg/kg/day in young dogs (equivalent to 150 times the maximum recommended daily adult ophthalmic dose) has been associated with these type of effects.

Care is necessary in patients with impaired hepatic or renal function, glucose-6-phosphate dehydrogenase deficiency, or myasthenia gravis.

Nervous system and psychiatric disorders (see **"SIDE EFFECTS"**) are more likely to occur in elderly patients and those with impaired renal function.

Corneal perforation has been reported in patients with pre-existing corneal epithelial defects or corneal ulcers, when treated with **OCTIN**.

Corneal precipitates have been reported during treatment with **OCTIN**.

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

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 such as **OCTIN** ovelenser an extended period in patients with extensive ocular surface disease.

Possible photophobic reactions may occur (see **"SIDE EFFECTS"**). Wearing sunglasses and avoiding prolonged exposure to bright light is advised.

Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see **CONTRAINDICATIONS**). Renal function should be assessed before initiating treatment, and monitored during treatment, with fluoroquinolones or ACE inhibitors/renin-angiotensin receptor blockers.

There is some evidence, although inconclusive, of a possible association between oral fluoroquinolone use and mitral valve and/or aortic valve regurgitation. A thorough cardiovascular examination including an echocardiogram, should be performed before oral fluoroquinolones are prescribed. Fluoroquinolones should not be prescribed to patients with mitral valve and/or aortic valve regurgitation (see **CONTRAINDICATIONS**).

Effects on the ability to drive and use machinery:

Transient blurring of vision may occur on instillation of **OCTIN**. Patients should be advised not to drive or operate hazardous machinery unless vision is clear.

INTERACTIONS:

Concurrent administration of a non-steroidal anti-inflammatory drug (NSAID), e.g. fenbufen, or theophylline, may potentiate the central nervous system stimulant effects of ofloxacin, as in **OCTIN**.

OCTIN should be used with caution in patients receiving medicines known to

prolong the QT interval (e.g. Class IA and III anti-dysrhythmics, tricyclic antidepressants, macrolide antimicrobials, antipsychotics) (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Concomitant use of fluoroquinolones and ACE inhibitors/reninangiotensin receptor blockers may precipitate acute kidney injury (see **CONTRAINDICATIONS**).

If concurrent use of these medicines is deemed necessary, they should be used with caution and the renal function should be monitored frequently throughout treatment.

HUMAN REPRODUCTION:

Pregnancy:

OCTIN is contraindicated during pregnancy (see **"CONTRAINDICATIONS"**).

Lactation:

OCTIN is not recommended for breastfeeding women. There is a potential harm for feeding infants since ofloxacin and other quinolones are excreted in breast milk.

DOSAGE AND DIRECTIONS FOR USE:

Do not touch the applicator tip to any surface (including the eye).

Keep the eyes closed for 1 – 2 minutes after application.

OCTIN should be used for the complete treatment period.

Treatment should not exceed 10 days.

Conjunctivitis:

Day 1 and 2:	1 drop every 2 – 4 hours.
Day 3 – 5:	1 drop every 6 hours.

Bacterial corneal ulcers:

Day 1 and 2:	1 – 2 drops into the affected eye(s) every 30 minutes while awake. 1 – 2 drops after 4 and 6 hours after retiring.
Day 3 – 7:	1 – 2 drops hourly while awake.
Day 7 – 9 or until completion:	1 – 2 drops 4 times daily.

Instructions for use:



SIDE EFFECTS:

Since small amounts of ofloxacin are systemically absorbed after ocular administration, side effects associated with systemic administration may occur. The following side effects have been reported:

Blood and lymphatic system disorders:

Frequency unknown: Blood dyscrasias (e.g. leucopenia, agranulocytosis, thrombocytopenia, and anaemia).

Immune system disorders:

Less frequent: Haemorrhagic conjunctivitis with palpebral oedema due to allergic reactions (see **"Eye disorders"**), hypersensitivity reactions affecting the skin (see **"Skin and subcutaneous tissue disorders"**), angioedema, dyspnoea, anaphylactic reaction (such as angioedema, dyspnea / shock, allergic derrmatitis, oropharyngeal swelling and swollen tongue (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Frequency unknown: Facial and glottal oedema, periorbital oedema.

Metabolism and nutrition disorders:

Less frequent: Hypoglycaemia, particularly in diabetic patients (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Psychiatric disorders:

Less frequent: Hallucinations, psychotic reactions (e.g. restlessness, agitation, anxiety, confusion), depression (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Frequency unknown: Sleep disturbances, nightmares.

Nervous system disorders:

Frequent: Headache, dizziness.

Less frequent: Convulsions.

Frequency unknown: Paraesthesia, peripheral neuropathy, tremor, unsteady gait, disturbances of the senses of taste and smell, epilepsy (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Eye disorders:

Frequent: Transient ocular irritation including burning, dryness, tearing, stinging, redness, itching, ocular discomfort.

Less frequent: Haemorrhagic conjunctivitis with palpebral oedema due to allergic reactions (see **"Immune system disorders"**).

Frequency unknown: Photophobia, visual disturbances (e.g. double and abnormal colour vision), conjunctivitis, blurred vision, periorbital oedema, foreign body sensation, increased lacrimation, dry eye, eye pain, ocular hyperaemia, hypersensitivity (including eye pruritus and eyelid pruritus – see **"Immune system disorders"**), keratitis, periorbital oedema.

Cardiac disorders:

Frequency unknown: Tachycardia, ventricular dysrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged.

Vascular disorders:

Frequency unknown: Vasculitis, ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation); ECG QT prolonged.

Gastrointestinal disorders:

Frequency unknown: Gastrointestinal disturbances including nausea, vomiting, diarrhoea, abdominal pain, and loss of appetite.

Hepato-biliary disorders:

Frequency unknown: Elevated liver enzyme values, jaundice, hepatitis.

Skin and subcutaneous tissue disorders:

Less frequent: Hypersensitivity reactions including rash, pruritus, vasculitis, petechiae, haemorrhagic bullae and papules, Stevens-Johnson syndrome, erythema multiforme, and toxic epidermal necrolysis (see **"Immune system disorders"**). Skin reactions on exposure to strong sunlight have also been reported (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Muscle and joint pain.

Renal and urinary disorders:

Less frequent: Acute renal failure.

Frequency unknown: Transient increases in serum creatinine or blood urea, crystalluria.

General disorders and administrative site disorders

Frequency unknown: Facial oedema

Post-marketing:

Metabolism and nutrition disorders:

Frequency unknown: Hyperglycaemia, hypoglycaemic coma (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Cardiac disorders:

Frequency unknown: Cases of mitral valve and/or aortic valve regurgitation were reported in patients treated with oral fluoroquinolones, such as **OCTIN**. Due to insufficient post-marketing information in the reported cases, it is unknown whether fluoroquinolone use was the causative factor, or a contributory factor or played no role in the reported cases where mitral and/or aortic regurgitation cases was diagnosed.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Following accidental ingestion, an increased potential for systemic side effects may be expected (see **"SIDE EFFECTS"**).

Topical overdosage may be treated with a topical ocular irrigant.

Treatment is symptomatic and supportive. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.

IDENTIFICATION:

A pale yellow, clear, sterile solution.

PRESENTATION:

Dropper bottles of 5 mℓ sterile solution.

STORAGE INSTRUCTIONS:

Preserve in tight, light-resistant container.

Store at or below 25 °C.

Do not use more than 30 days after opening.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

36/15.1/0002

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

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