PROFESSIONAL INFORMATION

OCUCON

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

OCUCON 5mg/mL eye drop solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL of solution contains moxifloxacin hydrochloride 5,45 mg equivalent to moxifloxacin 5 mg base.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye drops solution.

Clear, greenish-yellow solution, free from foreign particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

OCUCON is indicated for

- the topical treatment of bacterial conjunctivitis caused by susceptible organisms (see section 5.1)
- preoperative and postoperative sterilization for ophthalmic surgery

Changes in the international and local antimicrobial resistance patterns should also be a consideration.

4.2 Posology and method of administration

Posology

Use in adults including the elderly

Instil one drop in the affected eye(s) 3 times a day for 4 days.

No overall differences in safety and effectiveness have been observed between elderly and other adult patients.

Preoperative and postoperative sterilization

The recommended dose is one drop of OCUCON in the affected eye(s) 5 times per day for 2 days before ophthalmic surgery, and 3 times per day for 14 days after ophthalmic surgery.

Special populations

Use in hepatic and renal impairment

Pharmacokinetic parameters of oral moxifloxacin were not significantly altered in patients with mild to moderate hepatic insufficiency (Child Pugh Classes A and B).

Studies were not performed in patients with severe hepatic impairment (Child Pugh Class C).

Because of the low systemic exposure by the topical route of administration, no dosage adjustment of OCUCON is needed in patients with hepatic impairment.

The pharmacokinetic parameters of oral moxifloxacin are not significantly altered by mild, moderate or severe renal impairment. No dosage adjustment of OCUCON is necessary in patients with renal impairment.

Elderly population

No overall differences in safety and effectiveness have been observed between elderly and other adult patients.

Paediatric population

OCUCON has been shown to be safe and effective in paediatric patients including neonates and can be used at the same dose as in adults. There is no evidence that the ophthalmic administration of moxifloxacin as in OCUCON has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Method of administration

For ocular use only.

Not for injection. OCUCON should not be injected sub-conjunctivally or introduced directly into the anterior chamber of the eye.

To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle.

In order to prevent the drops from being absorbed via the nasal mucosa, particularly in new-born infants or children, the nasolacrimal ducts should be held closed for 2 to 3 minutes with the fingers after administering the drops. After cap is removed, if tamper evident snap collar is loose, remove before using the product.

If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.3 Contraindications

- History of hypersensitivity to moxifloxacin, to other quinolones, or to any of the excipients of OCUCON (see section 6.1)

4.4 Special warnings and precautions for use

Prescribers should adhere to the principles of antibiotic stewardship.

In patients receiving systemically administered quinolones, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, dyspnoea, urticaria, and itching (see section 4.8).

If an allergic reaction to OCUCON occurs, discontinue use of the medicine. Serious acute

hypersensitivity reactions to moxifloxacin or any other excipients may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Prolonged use of OCUCON may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including moxifloxacin, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration of moxifloxacin as in OCUCON plasma concentrations of moxifloxacin are much lower than after therapeutic oral doses of moxifloxacin, however, caution should be exercised and treatment with OCUCON should be discontinued at the first sign of tendon inflammation (see section 4.8).

OCUCON should not be used for the prophylaxis or empiric treatment of gonococcal conjunctivitis, including gonococcal ophthalmia neonatorum, because of the prevalence of fluoroquinolone-resistant *Neisseria gonorrhoeae*. Patients with eye infections caused by *Neisseria gonorrhoeae* should receive appropriate systemic treatment.

Patients should be advised not to wear contact lenses if they have signs and symptoms of a bacterial ocular infection.

Paediatric population

Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition, e.g. systemic treatment in cases caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae*.

OCUCON is not recommended for the treatment of *Chlamydia trachomatis* in patients less than 2 years of age as it has not been evaluated in such patients. Patients older than 2 years of age with eye infections caused by *Chlamydia trachomatis* should receive appropriate systemic treatment.

4.5 Interaction with other medicines and other forms of interaction

While medicine interaction studies have not been conducted with moxifloxacin as in OCUCON, they have been performed with the oral product at much higher systemic exposures than are achieved by the topical ocular route. Unlike some other fluoroquinolones, no clinically significant medicine interactions between systemically administered moxifloxacin and itraconazole, theophylline, warfarin, digoxin, oral contraceptives, probenecid, ranitidine or glyburide have been observed. *In vitro* studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19 or CYP1A2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of medicines metabolised by these cytochrome P450 isozymes.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

No information available.

Pregnancy

Since there are no adequate and well-controlled studies in pregnant women, OCUCON should be used during pregnancy with caution. However, no effects on pregnancy are anticipated since the systemic exposure to moxifloxacin from topical ocular application is negligible.

Breastfeeding

Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when OCUCON is administered to a nursing mother. However, at therapeutic doses of OCUCON, no effects on the suckling child are anticipated.

Fertility

Studies have not been performed to evaluate the effect of ocular administration moxifloxacin as in OCUCON on fertility.

4.7 Effects on ability to drive and use machines

Moxifloxacin has no or negligible influence on the ability to drive and use machines, however as with any eye drops, temporary blurred vision or other visual disturbances may occur with OCUCON which may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient should wait until their vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

No serious ophthalmic or systemic undesirable effects related to moxifloxacin eye drops were reported in any of the clinical studies conducted. The most frequently reported treatment-related undesirable effects with moxifloxacin eye drops were eye irritation and eye pain, occurring at an overall incidence of 1 to 2 %. These reactions were mild in 96 % of those patients who experienced them, with only 1 patient discontinuing therapy as a result.

Tabulated list of adverse effects

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	Less frequent	Haemoglobin decreased
Immune system disorders	Frequency unknown	Hypersensitivity reactions* accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, urticaria and itching

Metabolism and nutrition disorders	Less frequent	Taste perversion (altered bitter or bad taste following instillation)
Nervous system disorders	Less frequent Frequency unknown	Headache, paraesthesia Dizziness*
Eye disorders	Frequent Less frequent <

Cardiac disorders	Frequency unknown	Palpitations*
Respiratory, thoracic and mediastinal disorders	Less frequent Frequency unknown	Nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat) Dyspnoea*
Gastrointestinal disorders	Less frequent Frequency unknown	Vomiting, dysgeusia Nausea*
Hepatobiliary disorders	Less frequent	Alanine aminotransferase increased, gamma-glutamyl transferase increased
Skin and subcutaneous tissue disorders	Frequency unknown	Erythema*, rash*, pruritis*, urticaria*
Musculoskeletal, connective tissue and bone disorders	Frequency unknown	Tendon inflammation, tendon rupture

*Post marketing

a. Description of selected adverse reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following first dose, have been reported in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, dyspnoea, urticaria and itching (see section 4.4). Ruptures of the shoulder, hand, Achilles, or other tendons that required surgical repair or resulted in

prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and post marketing experience with systemic quinolones indicate that a risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress, including Achilles tendon (see section 4.4).

b. Paediatric population

In clinical trials, moxifloxacin has shown to be safe in paediatric patients, including neonates. In patients under 18 years old, the two most frequent adverse reactions were eye irritation and eye pain, both occurring at an incidence rate of 0,9%.

Based on data from clinical trials involving paediatric patients, including neonates, the type and severity of adverse reactions in the paediatric population are similar to those in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

The limited holding capacity of the conjunctival sac practically precludes any overdosing of OCUCON. Intoxication after inadvertent oral ingestion can also be ruled out.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmological; anti-infectives, other anti-infectives

ATC code: S01A E07

Pharmacological classification: A.15.1 Ophthalmic preparations with antibiotics and/or sulphonamides

Moxifloxacin is a fourth-generation fluoroquinolone antibacterial medicine active against a broad spectrum of Gram-positive and Gram-negative ocular pathogens, atypical microorganisms and anaerobes.

Mechanism of action

Moxifloxacin has *in vitro* activity against a wide range of Gram-positive and Gram-negative microorganisms. Moxifloxacin inhibits the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair and recombination. The C8-methoxy moiety of moxifloxacin also lessens the selection of resistant mutants of Gram-positive bacteria.

Mechanism(s) of Resistance

In vitro resistance to moxifloxacin develops slowly via multiple-step mutations and occurs at a general frequency between 10 - 9 to 10 - 11 for Gram-positive bacteria.

Fluoroquinolones, including moxifloxacin, differ in chemical structure and mode of action from ß-lactam antibiotics, macrolides and aminoglycosides, and therefore may be active against bacteria resistant to ß-lactam antibiotics, macrolides and aminoglycosides.

Susceptibility to Moxifloxacin

Aerobic Gram-positive micro-organisms

COMMONLY SUSCEPTIBLE SPECIES
Aerobic Gram-positive micro-organisms:
Corynebacterium species including *Corynebacterium diphtheriae*
Staphylococcus aureus (methicillin susceptible)

Streptococcus epidermidis

Streptococcus hominis

Streptococcus warneri

Streptococcus pneumoniae

Streptococcus pyogenes

Streptococcus viridans Group

Aerobic Gram-negative micro-organisms:

Acinetobacter species

Escherichia coli

Enterobacter cloacae

Haemophilus influenzae

Klebsiella oxytoca

Moraxella catarrhalis

Serratia marcescens

Anaerobic micro-organisms:

Proprionibacterium acnes

Other micro-organisms:

Chlamydia trachomatis

SPECIES FOR WHICH ACQUIRED RESISTANCE MAY BE A PROBLEM

Aerobic Gram-positive micro-organisms:

Staphylococcus aureus (methicillin resistant)

Staphylococcus, coagulase-negative species (methicillin resistant)

Aerobic Gram-negative micro-organisms:

Neisseria gonorrhoeae

Other micro-organisms:

None

INHERENTLY RESISTANT ORGANISMS

Aerobic Gram-negative micro-organisms:
Pseudomonas aeruginosa
Other micro-organisms:
None

5.2 Pharmacokinetic properties

Following topical ocular administration, moxifloxacin is absorbed into the systemic circulation (mean steady-state C_{max} and AUC were 2,7 ng/mL and 41,9 ng·hr/mL, respectively). These exposure values are approximately 1 600 and 1 200 times lower than the mean C_{max} and AUC following 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin is estimated to be 13 hours.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure following administration to the eye indicating little relevance to clinical use.

As with other quinolones, moxifloxacin was also genotoxic *in vitro* in bacteria and mammalian cells. As these effects can be traced to the interaction with bacterial gyrase and in considerably higher concentrations to the interaction with topoisomerase II in mammalian cells, a threshold level for genotoxicity can be assumed. In *in-vivo* tests, no evidence of genotoxicity was found, despite high doses of moxifloxacin. The therapeutic doses for human use therefore provide adequate safety margin. No indication of a carcinogenic effect was observed in an initiation promotion model in rats.

Unlike other quinolones, moxifloxacin showed no phototoxic or photo genotoxic properties in extensive *in vitro* and *in vivo* studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Boric acid

Sodium chloride

Sodium hydroxide (to adjust pH)

Water for injection

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 36 months

Opened: 28 days

6.4 Special precautions for storage

Use within 28 days of first opening.

Store at or below 30 °C.

6.5 Nature and contents of container

OCUCON is packed in a natural LDPE ophthalmic dispenser of 10 mL with a plastic LDPE transparent dropper insert and a white HDPE cap with a tamper proof seal containing 5 mL of eye drops solution.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER(S)

A51/15.1/0137

9. DATE OF FIRST AUTHORISATION

02 November 2021

10. DATE OF REVISION OF THE TEXT

07 February 2025