Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Mocin
Moxifloxacin ophthalmic solution 0.5% w/v

2. Qualitative and quantitative composition

1 ml of solution contains 5.45 mg Moxifloxacin hydrochloride equivalent to 5 mg Moxifloxacin base.

3. Pharmaceutical form

Clear, greenish-yellow solution.

4. Clinical particulars

4.1 Therapeutic indications

Mocin is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of bacteria to moxifloxacin.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Instill one drop in the affected eye 3 times a day for 7 days.
Children:
The safety and efficacy of Mocin in children under the age of 1 year has not been established. The dosage in children above the age of 1 year is the same as for adults.
Method of administration
For ocular use only. Not for injection. Moxifloxacin 0.5%w/v eye drops, solution should not be injected subconjunctivally 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

Mocin is contraindicated in patients with a history of hypersensitivity to Moxifloxacin, to other quinolones, or to any of the components in this medication.

4.4 Special warnings and precautions for use

Solution is for topical ophthalmic use only and should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye. As with other anti-infective, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining.
In general, patients with signs and symptoms of bacterial conjunctivitis should be advised not to wear contact lenses.
Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including Moxifloxacin, particularly in elderly patients and in those treated concurrently with corticosteroids. Treatment with MOCIN should be discontinued at the first sign of tendon inflammation.
There are no studies on the effect of ocular administration of MOCIN on fertility.

4.5 Interaction with other medicinal products and other forms of interaction

Drug-drug interaction studies have not been conducted with MOCIN eye drop. Moxifloxacin can be chelated by polyvalent ions such as Mg++, Al+++, Fe++ and Zn++. There is limited information available on the concurrent use of MOCIN eye drop and other ophthalmic products. Following oral administration, no clinically significant drug-drug interactions between theophylline, warfarin, digoxin, oral contraceptives or glyburide have been observed with Moxifloxacin. Theophylline, digoxin, probenecid, and ranitidine have been shown not to alter the pharmacokinetics of Moxifloxacin. 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 drugs metabolized by these cytochrome P450 isozymes.

4.6 Pregnancy and Lactation

Since there are no adequate and well-controlled studies in pregnant women MOCIN solution should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

Moxifloxacin is excreted in the breast milk of rats following oral and intravenous administration. Because of the potential for unknown effects from Moxifloxacin in infants being nursed by mothers taking MOCIN eye drop, a decision should be made to either discontinue nursing or discontinue the administration of MOCIN eye drop, taking into account the importance of MOCIN eye drop therapy to the mother and the possible risk to the infant

4.7 Effects on ability to drive and use machines

MOCIN may cause temporary blurred vision or other visual disturbances, which may affect the ability to drive or use machines. If blurred vision occurs at application, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

Summary of the safety profile
In clinical studies involving 2,252 patients, MOXIVIG was administered up to 8 times a day, with over 1,900 of these patients receiving treatment 3 times daily. The overall safety population that received the medicinal product consisted of 1,389 patients from the United States and Canada, 586 patients from Japan and 277 patients from India. No serious ophthalmic or systemic undesirable effects related to the medicinal product were reported in any of the clinical studies. The most frequently reported treatment-related undesirable effects with the medicinal product 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 summary of adverse reactions
The following adverse reactions are classified according to the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) or not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

System Organ Classification	Frequency	Adverse reactions

Blood and lymphatic system disorders	Rare	haemoglobin decreased
Immune system disorders	Not known	Hypersensitivity
Nervous system disorders	Uncommon Rare Not known	headache paresthesia dizziness
Eye disorders	Common Uncommon Rare Not known	eye pain, eye irritation punctate keratitis, dry eye, conjunctival haemorrhage, ocular hyperaemia, eye pruritus, eyelid oedema, ocular discomfort, corneal epithelium defect, corneal disorder, conjunctivitis, blepharitis, eye swelling, conjunctival oedema, vision blurred, visual acuity reduced, asthenopia, erythema of eyelid endophthalmitis, ulcerative keratitis, corneal erosion, corneal abrasion, intraocular pressure increased, corneal opacity, corneal infiltrates, corneal deposits, eye allergy, keratitis, corneal oedema, photophobia, eyelid oedema, lacrimation increased, eye discharge, foreign body sensation in eyes
Cardiac disorders	Not known	palpitations
Respiratory, thoracic and mediastinal disorders	Rare Not known	nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat) dyspnoea
Gastrointestional disorders	Uncommon Rare Not known	dysgeusia vomiting nausea

Hepatobiliary disorders	Rare	alanine aminotransferase increased, gammaglutamyltransferase increased
Skin and subcutaneous tissue disorders	Not known	erythema, rash, pruritus, urticaria

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).
Paediatric population
In clinical trials, MOXIVIG 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 (see section 5.1), 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 authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the Pharmacy and Poisons Board (PPB) through the Pharmacovigilance Electronic Reporting System (PvERS) at https://pv.pharmacyboardkenya.org/ or by using the approved PPB ADR reporting forms.

4.9 Overdose

In the event of acute over dosage MOCIN eye drops may be flushed from the eye(s) with warm tap water.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group
Ophthalmological; anti-infectives, other anti-infectives
ATC Code:
S01A E07
The antibacterial action of Moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division.
The mechanism of action for quinolones, including Moxifloxacin, is different from that of macrolides, aminoglycosides, or tetracyclines. Therefore, Moxifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to Moxifloxacin. There is no cross-resistance between Moxifloxacin and the aforementioned classes of antibiotics. Cross resistance has been observed between systemic Moxifloxacin and some other quinolones.
Moxifloxacin has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections.
Aerobic Gram-positive microorganisms:
Corynebacterium species, *Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus warneri, Streptococcus pneumonia, Streptococcus viridans* group.
Aerobic Gram-negative microorganisms:
Acinetobacter lwoffii, Haemophilus influenza, Haemophilus parainfluenzae.
Other microorganisms:
Chlamydia trachomatis

5.2 Pharmacokinetic properties

Plasma concentrations of Moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of MOCIN solution 3 times a day. The mean steady-state Cmax (2.7 ng/mL) and estimated daily exposure AUC (45 ng*hr/mL) values were 1,600 and 1,000 times lower than the mean Cmax and AUC reported after therapeutic 400 mg doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

Absorption Following 3 times daily dosing of moxifloxacin eye drops 0.5% solution to both eyes for five days (one dose on the 5th day); mean maximal steady-state plasma concentration (Cmax) and area under the plasma concentration time curve (AUC0-∞) of moxifloxacin was 2.7 ± 1.29 ng/mL ng/mL and 41.9 ± 15.6 ng*hr/mL, respectively. This Cmax value is 1667-fold lower and the AUC0-∞ value is 917-fold lower than the reported steady-state concentration and AUC0-∞ value after 400 mg oral doses of moxifloxacin. In a clinical pharmacokinetics study reported in the literature, oral absorption of moxifloxacin of healthy volunteers is rapid and the bioavailability is almost complete at 86%.

Distribution Moxifloxacin distributes into human tear film after topical ocular administration of 0.5% moxifloxacin. After 3 days of bilateral TID dosing, a peak tear concentration of moxifloxacin was 55.2 µg/mL and trough concentration after 1 day of bilateral TID dosing was 4.2 µg/mL. These values are above the minimum inhibitory concentrations for many of the common pathogens associated with bacterial conjunctivitis. Moxifloxacin does bind to melanin, resulting in a long half-life in the iris-ciliary body (pigmented rabbit) after ocular administration. Plasma protein binding of moxifloxacin is low with a reported unbound fraction of 55% in human males, which is independent of concentration over a wide concentration range (0.1 to 10 µg/mL).

Metabolism Moxifloxacin undergoes both sulfation of the secondary amine (M1), major pathway and glucuronidation of the carboxyl group (M2), secondary pathway in man. Sulfation occurs on the secondary amine of moxifloxacin while glucuronidation occurs on the carboxylic acid to form an acyl glucuronide. N-sulfonate and the acyl glucuronide are approximately one-third and one-tenth of parent drug maximal concentration after oral administration. Substantial percentage of the acyl glucuronide exposure after oral administration is the result of first-pass phase II metabolism. Neither the N-sulfonate metabolite nor the acyl glucuronide appeared to be pharmacologically active.

Elimination The reported systemic half-life of moxifloxacin after topical ocular administration is approximately 13 hours. After systemic administration of moxifloxacin, >95% of the dose was recovered in urine and feces. Fecal excretion was found to be the major route of elimination. Both parent drug (25% of the dose) and the N-sulfonate metabolite (35% of the dose) accounted for 60% of the total dose in feces. The acyl glucuronide was not detected in feces after systemic administration. Urinary excretion accounted for another 35% of the total dose with 20% as parent drug, 15% as the Nsulfonate metabolite and 5% as the acyl-glucuronide metabolite and the renal clearance

was 43 mL/min. Renal excretion is the result of glomerular filtration, active secretion (the acyl glucuronide metabolite) and tubular reabsorption.

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 photogenotoxic properties in extensive *in vitro* and *in vivo* studies.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sodium chloride
Boric acid
Hydrochloric acid and/or sodium hydroxide (to adjust pH)
Water for injection

6.2 Incompatibilities

None known

6.3 Shelf-Life

36 months
Discard 28 days after first opening

6.4 Special Precautions for storage

Store in a cool dry place below 30°C but do not freeze.
Keep out of the reach and sight of children.
Protect from light.

6.5 Nature and Content of container

Low density polyethylene dropper bottles and a white screw cap in pack sizes of 5mL and 10mL.

6.6 Special precautions for disposal and other handling

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures.
Discard the product in 28 days after first opening

7. Marketing Authorization Holder

Abacus Parenteral Drugs Limited Block 191, Plot no.114, Kinga Mukono P.O. Box 31376, Kampala, Uganda.
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8. Marketing Authorization Number

UGANDA: NDA/MAL/HDP/9725

9. Date of first authorization/renewal of the authorization

5th Oct 2021

10. Date of revision of the text

10 October 2024