PROFESSIONAL INFORMATION LEAFLET: GENFLOC®

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

GENFLOC® 5 mg/ml Ophthalmic Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains moxifloxacin hydrochloride equivalent to 5 mg of the moxifloxacin free base. Sterile solution.
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Ophthalmic Solution.
Yellow coloured, clear solution, free from visible particles of foreign matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GENFLOC is indicated for the topical treatment of bacterial conjunctivitis caused by susceptible organisms (see section 5.1 for susceptibility to moxifloxacin).

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 between elderly and other adult patients have been observed with GENFLOC.

Special populations:

Use in hepatic 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 administration, no dosage adjustment of GENFLOC is needed in patients with hepatic impairment.

Use in renal impairment:

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

Paediatric population:

GENFLOC 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 GENFLOC 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.

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.

4.3 Contraindications

GENFLOC is contraindicated in patients with a history of hypersensitivity to the active substance moxifloxacin, to other quinolones or to any of the excipients of GENFLOC listed in section 6.1.

4.4 Special warnings and precautions for use

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 GENFLOC occurs, discontinue use of the medicine. Serious acute hypersensitivity reactions to moxifloxacin or any other ingredient may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated.

Prolonged use 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 as in GENFLOC, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration, plasma concentrations of moxifloxacin are much lower than after therapeutic oral doses of moxifloxacin (see section 4.5 and 5.2), however, caution should be exercised and treatment with GENFLOC should be discontinued at the first sign of tendon inflammation (see section 4.8).

GENFLOC 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*.

GENFLOC 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 interaction studies have not been conducted with moxifloxacin ophthalmic solution, they have been performed with the oral dosage form at much higher systemic exposures than are achieved by the topical ocular route. No clinically significant 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 as in GENFLOC is unlikely to alter the pharmacokinetics of medicines metabolised by these cytochrome P450 isozymes.

Given the low systemic concentration of moxifloxacin following topical ocular administration (see Section 5.2), interactions are unlikely to occur.

4.6 Pregnancy and lactation
Pregnancy:
Since there are no adequate and well-controlled studies in pregnant women, GENFLOC should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

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 GENFLOC is administered to a nursing mother.

Fertility:

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

4.7 Effects on ability to drive and use machines

Temporary blurred vision or other visual disturbances may occur with GENFLOC. Patients should be advised to wait until their vision clears before driving or using machinery if they experience blurred vision at instillation.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	**GENFLOC Side Effects**
Blood and lymphatic system disorders	
Less frequent:	haemoglobin decreased
Immune system disorders	
Less frequent:	hypersensitivity
Nervous system disorders	
Less frequent:	headache, paraesthesia, dizziness
Eye disorders	
Frequent:	eye pain, eye irritation
Less frequent:	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, blurred vision, reduced visual acuity, asthenopia, erythema of eyelid endophthalmitis, ulcerative keratitis, corneal erosion, corneal abrasion, increased intraocular pressure, corneal opacity, corneal

	infiltrates, corneal deposits, eye allergy, keratitis, corneal oedema, photophobia, eyelid oedema, increased lacrimation, eye discharge, foreign body sensation in eyes
Cardiac disorders	
Less frequent:	palpitations
Respiratory, thoracic and mediastinal disorders	
Less frequent:	nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat), dyspnoea
Gastrointestinal disorders	
Less frequent:	Dysgeusia, vomiting, nausea
Hepatobiliary disorders	
Less frequent:	increased alanine aminotransferase, increased gamma-glutamyltransferase
Skin and subcutaneous tissue disorders	
Less frequent:	erythema, rash, pruritus, urticaria

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 providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8.
In addition, suspected adverse reactions can be reported to Gen-Eye (Pty) Ltd via email: pharmacovigilance@gen-eye.co.za or telephonically on 011 312 3812.

4.9 Overdose

The limited holding capacity of the conjunctival sac for ophthalmic medicines practically precludes any overdosing of GENFLOC. Intoxication after inadvertent oral ingestion can also be ruled out. The total amount of moxifloxacin in a single container is too small to induce adverse effects after accidental ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification:

15.1 Ophthalmic preparations with antibiotics and/or sulphonamides.

Mechanism of action:

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

Resistance:

Resistance to fluoroquinolones, including moxifloxacin generally occurs by chromosomal mutations in genes encoding DNA gyrase and topoisomerase IV. In Gram-negative bacteria, moxifloxacin resistance can be due to mutations in *mar* (multiple antibiotic resistance) and the *qnr* (quinolone resistance) gene systems. Resistance is also associated with expression of bacteria efflux proteins and inactivating enzymes. Cross-resistance with beta-lactams, macrolides and aminoglycosides is not expected due to differences in mode of action.

COMMONLY SUSCEPTIBLE SPECIES
Aerobic Gram-positive micro-organisms:
Corynebacterium species including
Corynebacterium diphtheriae
Staphylococcus aureus (methicillin susceptible)
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus viridans Group
Aerobic Gram-negative micro-organisms:
Enterobacter cloacae
Haemophilus influenzae

Klebsiella oxytoca *Moraxella catarrhalis* *Serratia marcescens* **Anaerobic micro-organisms:** *Propionibacterium 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

It was reported that following ocular administration of moxifloxacin as in GENFLOC, moxifloxacin was absorbed into the systemic circulation. The mean steady state C_{max} and AUC following bilateral administration of ocular doses of moxifloxacin three times a day for 4 days 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 reported after therapeutic 400 mg oral doses of moxifloxacin. Moxifloxacin has an estimated plasma half-life of approximately 13 hours.

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

Not applicable.

6.3 Shelf life

Unopened: 2 years

Opened: 28 days

6.4 Special precautions for storage

Store at or below 25 °C. Keep the container well-closed and in the outer carton. Protect from light. Discard 28 days after first opening (see section 6.3).

6.5 Nature and contents of container

5 ml translucent low-density polyethylene vial, with a translucent low-density polyethylene nozzle and a white high-density polyethylene cap enclosed in a carton.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Gen-Eye (Pty) Ltd[1]
Royal Palm Business Estate
Unit 7, 646 Washington Street
Halfway House, Midrand, 1685

8. REGISTRATION NUMBER(S)

49/15.1/0909

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

08 December 2020

10. DATE OF REVISION OF THE TEXT

Not applicable

® GENFLOC is a registered trademark of Gen-Eye (Pty) Ltd.

[1] Company Registration number.: 2009/009360/07

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