National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. Name of the Medicinal Product

(a) Product Name : MOXIFORTE EYE DROPS
(b) Strength : 0.5 % w/v
(c) Pharmaceutical Dosage Form : Opthalmic Solution

2. Quality and Quantitative Composition

(a) Qualitative Declaration, the active substance should be declared by its recommended INN. Accompanied by its salt or hydrate form if relevant.

Composition:

Moxifloxacin Hydrochloride	BP	
Eq. to Moxifloxacin		0.5% w/v
Benzalkonium Chloride Solution (As Preservative)	B.P.	0.02% w/v
Sterile Aqueous Base	q.s	

(b) Quantitative Declaration, the quantity of the active substance must be expressed per dosage unit

Sr. No.	Name of the Materials	Specification	Label Claim	Quantity (mg/mL)	Active/ Inactive
1	Moxifloxacin Hydrochloride Eq. to Moxifloxacin	B.P.	0.5% w/v	54.50 mg	Active

3. Pharmaceutical Form Visual description of the appearance of the product (colour, markings, etc.) e.g.: Yellowish colour solution filled in sterile pet vial.

4. Clinical Particulars

4.1 Therapeutic Indications:

MOXIFORTE Eye Drops is indicated for the topical treatment of purulent bacterial conjunctivitis, caused by moxifloxacin susceptible strains.

4.2 Posology and method of administration:

Posology:

Use in adults including the elderly (≥ 65 years)
The dose is one drop in the affected eye(s) 3 times a day.

The infection normally improves within 5 days and treatment should then be continued for a further 2-3 days. If no improvement is observed within 5 days of initiating therapy, the diagnosis and/or treatment should be reconsidered. The duration of treatment depends on the severity of the disorder and on the clinical and bacteriological course of infection.

Paediatric patients

No dosage adjustment is necessary.

Use in hepatic and renal impairment

No dosage adjustment is necessary.

For ocular use only. Not for injection. MOXIFORTE 0.5% w/v eye drops, solution should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye.

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.

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.

Method of administration:
For ocular administration.

4.3 Contraindications:
Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warning 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.

If an allergic reaction to MOXIFORTE occurs, discontinue use of the medicinal product. Serious acute hypersensitivity reactions to moxifloxacin or any other product ingredient may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated.

As with other anti-infectives, 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, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration of MOXIFORTE plasma concentrations of moxifloxacin are much lower than after therapeutic oral doses of moxifloxacin, however, caution should be exercised and treatment with MOXIFORTE should be discontinued at the first sign of tendon inflammation.

Data are very limited to establish efficacy and safety of MOXIFORTE in the treatment of conjunctivitis in neonates. Therefore use of this medicinal product to treat conjunctivitis in neonates is not recommended.

MOXIFORTE 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.

The medicinal product 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 trachomitis should receive appropriate systemic treatment.

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

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

4.5 Interaction with other medicinal products and other forms of interactions:
No specific interaction studies have been performed with MOXIFORTE 0.5%w/v eye drops, solution. Given the low systemic concentration of moxifloxacin following topical ocular administration of the medicinal product (see Section 5.2), drug interactions are unlikely to occur.

4.6 Pregnancy and lactation:

Pregnancy
There are no adequate data from the use of MOXIFORTE in pregnant women. However, no effects on pregnancy are anticipated since the systemic exposure to moxifloxacin is negligible. The medicinal product can be used during pregnancy.

Breastfeeding
It is unknown whether moxifloxacin/metabolites are excreted in human milk. Animal studies have shown excretion of low levels in breast milk after oral administration of moxifloxacin. However, at therapeutic doses of MOXIFORTE no effects on the suckling child are anticipated. The medicinal product can be used during breast-feeding.

4.7 Effects on ability to drive and use machine:
MOXIFORTE 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 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 machinery.

4.8 Undesirable effects
The adverse reactions listed below 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, adverse reactions are presented in order of decreasing seriousness.

Blood and lymphatic system disorders:
Rare: haemoglobin decreased

Immune system disorders:
Not known: hypersensitivity

Nervous system disorders:

Uncommon: headache
Rare: paresthesia
Not known: dizziness

Eye disorders:
Common: eye pain, eye irritation
Uncommon: punctate keratitis, dry eye, conjunctival haemorrhage, ocular hyperaemia, eye pruritus, eyelid oedema, ocular discomfort
Rare: corneal epithelium defect, corneal disorder, conjunctivitis, blepharitis, eye swelling, conjunctival oedema, vision blurred, visual acuity reduced, asthenopia, erythema of eyelid
Not known: 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: nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat)
Not known: dyspnoea

Gastrointestional disorders:
Uncommon: dysgeusia
Rare: vomiting
Not known: nausea

Hepatobiliary disorders:
Rare: alanine aminotransferase increased, gamma-glutamyltransferase increased

Skin and subcutaneous tissue disorders:
Not known: erythema, rash, pruritus, urticarial

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.

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.

Paediatric population
In clinical trials, Moxifloxacin Ophthalmic Solution 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

4.9 Overdose:
The limited holding capacity of the conjunctival sac for ophthalmic products practically precludes any overdosing of the medicinal product.

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:

Pharmacotherapeutic group: Ophthalmologicals; anti-infectives, other anti-infectives. ATC code: S01A E07

Mechanism of Action:

Moxifloxacin, a fourth-generation fluoroquinolone, inhibits the DNA gyrase and topoisomerase IV required for bacterial DNA replication, repair, and recombination.

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.

Susceptibility Testing Breakpoints

There are no pharmacological data correlated with clinical outcome for moxifloxacin administered as a topical agent. As a result, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) suggests the following epidemiological cut-off values (ECOFF mg/l) derived from MIC distribution curves to indicate susceptibility to topical moxifloxacin:

Corynebacterium	ND
Staphylococcus aureus	0.25 mg/l
Staphylococcus, coag-neg.	0.25 mg/l
Streptococcus pneumoniae	0.5 mg/l
Streptococcus pyogenes	0.5 mg/l
Streptococcus, viridans group	0.5 mg/l
Enterobacter spp.	0.25 mg/l
Haemophilus influenzae	0.125 mg/l
Klebsiella spp.	0.25 mg/l
Moraxella catarrhalis	0.25 mg/l
Morganella morganii	0.25 mg/l
Neisseria gonorrhoeae	0.032 mg/l
Pseudomonas aeruginosa	4 mg/l
Serratia marcescens	1 mg/l

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of moxifloxacin in at least some types of infections is questionable.

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:
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 was absorbed into the systemic circulation. Plasma concentrations of moxifloxacin were measured in 21 male and female subjects who received bilateral topical ocular doses of the medicinal product 3 times a day for 4 days. The mean steady-state Cmax 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 Cmax and AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was 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 photogenotoxic properties in extensive in vitro and in vivo studies.

6 Pharmaceutical Particulars

6.1 List of excipients:

S. No.	Name of the Materials	Specification
1	Benzalkonium Chloride Solution	B.P.
2	Sodium Chloride	B.P.
3	Glycerin	B.P.
4	Disodium Edetate	B.P.
5	Sodium Hydroxide	B.P.
6	Water for Injections	B.P.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

The shelf-life is 24 Months for the unopened vial. The vial should be placed back in the original pack after each use.

6.4 Special precautions for storage: Store in cool, dark & dry place.

Store in a dark & dry place below 30°C. Do not allow to freeze.

6.5 Nature and contents of container:

10 ml white colour pet vial. Such 1 pet vial packed in a printed carton with pack insert.

6.6 Special precaution for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7.0 Applicant/Manufacturer

Name : ZEE LABORATORIES LIMITED

Address : Behind 47, Industrial Area, Paonta Sahib-173025 (INDIA)

Phone : 91-1704-265132

Fax : 91-1704-265135

E-mail : info@zeelab.co.in