

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

[Invented name], 5 mg/ml, eye drops, solution

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 5.45 mg moxifloxacin hydrochloride equivalent to 5 mg moxifloxacin base.

Each eye drop contains 0.2 mg of moxifloxacin.

For the full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Eye drops, solution

Green-yellow transparent solution

pH: 6.5 - 7.2

Osmolality: 275 - 310 mosmol/kg

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Topical treatment of purulent bacterial conjunctivitis, caused by moxifloxacin susceptible strains (see sections 4.4 and 5.1). Consideration should be given to official guidance on the appropriate use of antibacterial agents.

#### 4.2 Posology and method of administration

##### Posology

Ocular use.

##### Use in adults including the elderly ( $\geq 65$ 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.

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 it 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

Hypersensitivity to the active substance, other quinolones or to any of the excipients 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 [Invented name] 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 an 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 [Invented name] 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 [Invented name] should be discontinued at the first sign of tendon inflammation (see section 4.8).

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

Moxifloxacin 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 trachomatis* 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 trachomatis* 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 interaction

No specific interaction studies have been performed with moxifloxacin 5 mg/ml eye drops, solution.

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

#### 4.6 Fertility, pregnancy and lactation

##### Pregnancy

There are no adequate data from the use of moxifloxacin 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 is excreted in human breast milk. Animal studies have shown excretion of low levels in breast milk after oral administration of moxifloxacin. However, at therapeutic doses of moxifloxacin no effects on the suckling child are anticipated. The medicinal product can be used during breast-feeding.

##### Fertility

Studies have not been performed to evaluate the effect of ocular administration of moxifloxacin 5 mg/ml eye drops on fertility.

#### 4.7 Effects on ability to drive and use machines

[Invented name] 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

##### Summary of the safety profile

In clinical studies involving 2,252 patients, moxifloxacin 5 mg/ml eye drops, solution 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.

The following undesirable effects were assessed to be treatment-related and are classified according to the following convention: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  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<br>Rare<br>Not known | headache<br>paresthesias<br>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   |
| Gastrointestinal 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, 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, moxifloxacin 5 mg/ml eye drops, 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 (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 authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **the national reporting system** listed in [Appendix V](#).

## **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.

#### Mechanisms of resistance:

Resistance to fluoroquinolones, including moxifloxacin, occurs generally 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. 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:

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

#### Susceptibility:

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:**

*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

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 moxifloxacin 3 times a day for 4 days. The 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 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**

Sodium chloride  
Boric acid  
Sodium hydroxide (for pH-adjustment)  
Water purified

## **6.2 Incompatibilities**

Not applicable.

## **6.3 Shelf life**

2 years  
Discard 28 days after the first opening of the bottle.

## **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

After first opening of the bottle - store for 28 days at a temperature below 30°C.

## **6.5 Nature and contents of container**

LDPE 5 ml bottle closed with white LDPE dropper and white HDPE tamper proof closure.

## **6.6 Special precautions for disposal and other handling**

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

## **7. MARKETING AUTHORISATION HOLDER**

[To be completed nationally]

## **8. MARKETING AUTHORISATION NUMBER(S)**

[To be completed nationally]

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

[To be completed nationally]

## **10. DATE OF REVISION OF THE TEXT**

[To be completed nationally]