BASILOX 0.5%

Eye Drops

Composition
Moxifloxacin 0.5% (5 mg/ml)

Action
BASILOX 0.5 Eye Drops contains the fourth-generation fluoroquinolone, Moxifloxacin. Moxifloxacin has *in vitro* activity against a wide range of Gram-positive and Gram-negative micro-organisms. 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 compared to the C8-H moiety found in older fluoroquinolones. Moxifloxacin's bulky C-7 substituent group interferes with the quinolone efflux pump mechanism of bacteria. Moxifloxacin is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations.

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.

In vitro resistance to Moxifloxacin develops via multiple-step mutations. Resistance to Moxifloxacin occurs *in vitro* at a general frequency of between 1.8×10^{-9} to $< 1 \times 10^{-11}$ for Gram-positive bacteria.

Moxifloxacin has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as:

Aerobic Gram-positive Mmicroorganisms
Corynebacterium species*
*Micrococcus luteus**
Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus hominis
*Staphylococcus warneri**
Streptococcus pneumoniae
Streptococcus viridans group

Aerobic Gram-negative Microorganisms
*Acinetobacter lwoffii**
Haemophilus influenzae
*Haemophilus parainfluenzae**

Other Microorganisms
Chlamydia trachomatis
*Efficacy for this organism was studied in fewer than 10 infections.

The following *in vitro* data are also available, **but their clinical significance in ophthalmic infections is unknown**. The safety and effectiveness of BASILOX solution in treating ophthalmological infections due to these microorganisms have not been established in adequate and well-controlled trials.

The following organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the in vitro systemic breakpoint and ophthalmological efficacy has not been established. The list of organisms is provided as guidance only in assessing the potential treatment of conjunctival infections. Moxifloxacin exhibits in vitro minimal inhibitory concentrations

(MICs) of 2 µg/ml or less (systemic susceptible breakpoint) against most (≥ 90%) strains of the following ocular pathogens.

Aerobic Gram-positive Microorganisms
Listeria monocytogenes
Staphylococcus saprophyticus
Streptococcus agalactiae
Streptococcus mitis
Streptococcus pyogenes
Streptococcus Group C, G and F

Aerobic Gram-negative Microorganisms
Acinetobacter baumannii
Acinetobacter calcoaceticus
Citrobacter freundii
Citrobacter koseri
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Klebsiella oxytoca
Klebsiella pneumoniae
Moraxella catarrhalis
Morganella morganii
Neisseria gonorrhoeae
Proteus mirabilis
Proteus vulgaris
Pseudomonas stutzeri

Anaerobic Microorganisms
Clostridium perfringens
Fusobacterium species
Prevotella species
Propionibacterium acnes

Other Microorganisms
Chlamydia pneumoniae
Legionella pneumophila
Mycobacterium avium
Mycobacterium marinum
Mycoplasma pneumoniae

Pharmacokinetics
Plasma concentrations of Moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of Moxifloxacin solution 3 times a day. The mean steady-state Cmax (2.7 ng/mL) and estimated daily exposure AUC (45 ngâ€¢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.

Indications
Topical treatment of purulent bacterial conjunctivitis, caused by Moxifloxacin susceptible strains Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Contraindications
Hypersensitivity to the active substance, to other quinolones, or any other ingredients in this product.

Warnings & Precautions

Hypersensitivity Reaction
In patients receiving systemically administered quinolones, including Moxifloxacin, 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 edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to Moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Growth Of Resistant Organisms With Prolonged Use
As with other anti-invectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If super infection 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.

Avoidance Of Contact Lens Wear
Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis.

Use In Specific Populations
Pregnancy :Pregnancy Category C.

Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose); however, decreased fetal body weights and slightly delayed fetal skeletal development were observed. There was no evidence of teratogenicity when pregnant Cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (approximately 4,300 times the highest recommended total daily human ophthalmic dose). An increased incidence of smaller fetuses was observed at 100 mg/kg/day.

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

Nursing Mothers
Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when Moxifloxacin solution is administered to a nursing mother.

Pediatric Use
The safety and effectiveness of Moxifloxacin solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of Moxifloxacin solution has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Geriatric Use
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

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, 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.

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 .

Drug Interactions

Drug-drug interaction studies have not been conducted with Moxifloxain solution. 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.

Dosage and Administration

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

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.

Pediatric 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 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.

Presentation
Dropper bottle of 5 ml