**HIGHLIGHTS OF PRESCRIBING INFORMATION**

**These highlights do not include all the information needed to use Moxifloxacin Ophthalmic Solution USP, 0.5% safely and effectively. See full prescribing information for Moxifloxacin Ophthalmic Solution USP, 0.5%.**

**MOXIFLOXACIN Ophthalmic Solution USP, 0.5%**
**Sterile topical ophthalmic solution**
**Initial U.S. Approval: 1999**

**----------INDICATIONS AND USAGE----------**

Moxifloxacin Ophthalmic Solution USP is a topical fluoroquinolone anti-infective indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

*Aerococcus viridans*, Corynebacterium macginleyi*, Enterococcus faecalis*, Micrococcus luteus*, Staphylococcus arlettae*, Staphylococcus aureus, Staphylococcus capitis, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus saprophyticus*, Staphylococcus warneri*, Streptococcus mitis*, Streptococcus pneumoniae, Streptococcus parasanguinis*, Escherichia coli*, Haemophilus influenzae, Klebsiella pneumoniae*, Propionibacterium acnes, Chlamydia trachomatis**

*Efficacy for this organism was studied in fewer than 10 infections. (1)

**----------DOSAGE AND ADMINISTRATION----------**

Instill 1 drop in the affected eye(s) 2 times daily for 7 days. (2)

**----------DOSAGE FORMS AND STRENGTHS----------**

5 mL bottle filled with 3 mL sterile ophthalmic solution of moxifloxacin 0.5%. (3)

**----------CONTRAINDICATIONS----------**

None. (4)

**----------WARNINGS AND PRECAUTIONS----------**

- Topical ophthalmic use only. (5.1)
- Hypersensitivity and anaphylaxis have been reported with systemic use of moxifloxacin. (5.2)
- Prolonged use may result in overgrowth of non-susceptible organisms, including fungi. (5.3)
- Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis. (5.4)

**----------ADVERSE REACTIONS----------**

The most common adverse reactions reported in 1 to 2% of patients were eye irritation, pyrexia, and conjunctivitis. (6)

**To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceuticals, Inc at 1-800-399-2561 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 01/2019**

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**FULL PRESCRIBING INFORMATION: CONTENTS***



*Sections or subsections omitted from the full prescribing information are not listed.

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## FULL PRESCRIBING INFORMATION

## 1 INDICATIONS AND USAGE

Moxifloxacin ophthalmic solution USP is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

*Aerococcus viridans**
*Corynebacterium macginleyi**
*Enterococcus faecalis**
*Micrococcus luteus**
*Staphylococcus arlettae**
*Staphylococcus aureus*
*Staphylococcus capitis*
*Staphylococcus epidermidis*
*Staphylococcus haemolyticus*
*Staphylococcus hominis*
*Staphylococcus saprophyticus**
*Staphylococcus warneri**
*Streptococcus mitis**
*Streptococcus pneumoniae*
*Streptococcus parasanguinis**
*Escherichia coli**
*Haemophilus influenzae*
*Klebsiella pneumoniae**
*Propionibacterium acnes*
*Chlamydia trachomatis**

*Efficacy for this organism was studied in fewer than 10 infections.

## 2 DOSAGE AND ADMINISTRATION

Instill 1 drop in the affected eye(s) 2 times daily for 7 days.

## 3 DOSAGE FORMS AND STRENGTHS

5 mL bottle filled with 3 mL of sterile ophthalmic solution of moxifloxacin 0.5%.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Topical Ophthalmic Use Only

NOT FOR INJECTION. Moxifloxacin ophthalmic solution is for topical ophthalmic use only and should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye.

### 5.2 Hypersensitivity Reactions

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.

### 5.3 Growth of Resistant Organisms with Prolonged Use

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. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining.

### 5.4 Avoidance of Contact Lens Wear

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis.

## 6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to moxifloxacin ophthalmic solution in 1263 patients, between 4 months and 92 years of age, with signs and symptoms of bacterial conjunctivitis. The most frequently reported adverse reactions were eye irritation, pyrexia and conjunctivitis, reported in 1 to 2% of patients.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 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 25,000 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 5,000 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 ophthalmic solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

### 8.3 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 ophthalmic solution is administered to a nursing mother.

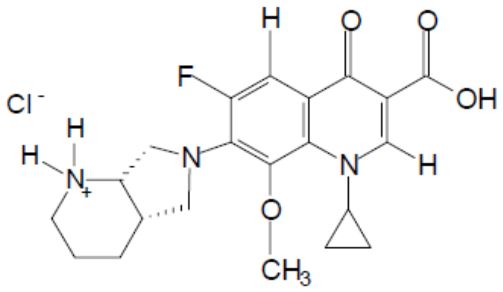
### 8.4 Pediatric Use
The safety and effectiveness of moxifloxacin ophthalmic solution in infants below 4 months of age have not been established.

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

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

## 11 DESCRIPTION
Moxifloxacin ophthalmic solution USP is a sterile solution for topical ophthalmic use.

Moxifloxacin hydrochloride is an 8-methoxy fluoroquinolone anti-infective, with a diazabicyclononyl ring at the C7 position.




$C_{21}H_{24}FN_3O_4 \cdot HCl$ Molecular Weight: 437.9

Chemical Name: 1-Cyclopropyl-6-fluoro-1,4-dihydro-8- methoxy-7- [(4aS,7aS)-octahydro- 6H-pyrrolol [3,4-b] pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride.

Each mL of moxifloxacin ophthalmic solution USP, 0.5 % contains 5.45 mg moxifloxacin hydrochloride USP, equivalent to 5 mg moxifloxacin base.

Inactives: boric acid, sodium chloride, sorbitol, tyloxapol, xanthan gum, hydrochloric acid and/or sodium hydroxide to adjust pH, and water for injection.

Moxifloxacin ophthalmic solution USP, 0.5% is a greenish-yellow, isotonic solution with an osmolality of 300 to 370 mOsm/kg and a pH of approximately 7.4. Moxifloxacin hydrochloride is a slightly yellow to yellow crystalline powder.

USP pH and Osmolality tests are pending.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Moxifloxacin is a member of the fluoroquinolone class of anti-infective drugs *[see CLINICAL PHARMACOLOGY (12.4)]*.

### 12.3 Pharmacokinetics

Moxifloxacin steady-state plasma pharmacokinetics were evaluated in healthy adult male and female subjects who were administered multiple, bilateral, topical ocular doses of moxifloxacin ophthalmic solution two times daily for four days with a final dose on day 5. The average steady-state $AUC_{0 \text{ to } 12}$ was 8.17 ± 5.31 ng*h/mL. Moxifloxacin $C_{max}$ following twice-daily bilateral ophthalmic administration of moxifloxacin 0.5% for 5 days is approximately 0.02% of that achieved with the oral formulation of moxifloxacin hydrochloride ($C_{max}$ following oral dosing of 400 mg AVELOX®, 4.5 ± 0.5 mcg/mL).

### 12.4 Microbiology

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.

*In vitro* resistance to moxifloxacin develops via multiple-step mutations. Resistance to moxifloxacin occurs *in vitro* at a general frequency of between $1.8 \times 10^{-9}$ 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 described in the **INDICATIONS AND USAGE** section:

*Aerococcus viridans**
*Corynebacterium macginleyi**
*Enterococcus faecalis**
*Micrococcus luteus**
*Staphylococcus arlettae**

*Staphylococcus aureus*
*Staphylococcus capitis*
*Staphylococcus epidermidis*
*Staphylococcus haemolyticus*
*Staphylococcus hominis*
*Staphylococcus saprophyticus**
*Staphylococcus warneri**
*Streptococcus mitis**
*Streptococcus pneumoniae*
*Streptococcus parasanguinis**
*Escherichia coli**
*Haemophilus influenzae*
*Klebsiella pneumoniae**
*Propionibacterium acnes*
*Chlamydia trachomatis**

*Efficacy for this organism was studied in fewer than 10 infections.

The following *in vitro* data are available, but their clinical significance in ophthalmic infections is unknown. The safety and effectiveness of moxifloxacin ophthalmic solution in treating ophthalmic infections due to these organisms have not been established in adequate and well-controlled trials.
Moxifloxacin has been shown to be active *in vitro* against most strains of the microorganisms listed below. These organisms are considered susceptible when evaluated using systemic breakpoints; however, a correlation between the *in vitro* systemic breakpoint and ophthalmologic 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 mcg/mL or less (systemic susceptible breakpoint) against most (≥90%) strains of the following ocular pathogens.

***Aerobic Gram-Positive Microorganisms***
*Staphylococcus caprae*
*Staphylococcus cohnii*
*Staphylococcus lugdunensis*
*Staphylococcus pasteuri*
*Streptococcus agalactiae*
*Streptococcus milleri* group
*Streptococcus oralis*
*Streptococcus pyogenes*
*Streptococcus salivarius*
*Streptococcus sanguis*

***Aerobic Gram-Negative Microorganisms***
*Acinetobacter baumannii*
*Acinetobacter calcoaceticus*
*Acinetobacter junii*

*Enterobacter aerogenes*
*Enterobacter cloacae*
*Haemophilus parainfluenzae*
*Klebsiella oxytoca*
*Moraxella catarrhalis*
*Moraxella osloensis*
*Morganella morganii*
*Neisseria gonorrhoeae*
*Neisseria meningitides*
*Pantoea agglomerans*
*Proteus vulgaris*
*Pseudomonas stutzeri*
*Serratia liquefaciens*
*Serratia marcescens*
*Stenotrophomonas maltophilia*

***Anaerobic Microorganisms***
*Clostridium perfringens*
*Peptostreptococcus anaerobius*
*Peptostreptococcus magnus*
*Peptostreptococcus micros*
*Peptostreptococcus prevotii*

***Other Microorganisms***
*Mycobacterium tuberculosis*
*Mycobacterium avium*
*Mycobacterium kansasii*
*Mycobacterium marinum*

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed.

Moxifloxacin was not mutagenic in four bacterial strains used in the Ames *Salmonella* reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity *in vivo* in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 25,000 times the highest recommended total daily human ophthalmic dose. At 500 mg/kg orally there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

## 14 CLINICAL STUDIES

In one randomized, double-masked, multicenter, vehicle-controlled clinical trial in which patients with bacterial conjunctivitis were dosed with moxifloxacin ophthalmic solution 2 times a day, moxifloxacin ophthalmic solution was superior to its vehicle for both clinical and microbiological outcomes. Clinical cure achieved on Day 4 was 63% (265/424) in moxifloxacin ophthalmic solution treated patients, versus 51% (214/423) in vehicle treated patients. Microbiologic success (eradication of baseline pathogens) was achieved on Day 4 in 75% (316/424) of moxifloxacin ophthalmic solution treated patients versus 56% (237/423) of vehicle treated patients. Microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Moxifloxacin ophthalmic solution USP, 0.5% is supplied as a sterile ophthalmic solution in a sterile 5 mL natural low density polyethylene bottle fitted with a natural low density polyethylene nozzle and sealed with a tan coloured high density polyethylene cap as follows:

3 mL in a 5 mL bottle (NDC 68180-421-01)

Storage: Store at 2° to 25°C (36° to 77°F).

## 17 PATIENT COUNSELING INFORMATION

### 17.1 Avoid Contamination of the Product

Advise patients not to touch the dropper tip to any surface to avoid contaminating the contents.

### 17.2 Avoid Contact Lens Wear

Advise patients not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

### 17.3 Hypersensitivity Reactions

Systemically administered quinolones, including moxifloxacin, have been associated with hypersensitivity reactions, even following a single dose. Advise patients to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.

AVELOX® is the registered trademark of the Bayer AG and is not the trademark of Lupin Limited.

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Baltimore, Maryland 21202
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Manufactured by:
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