Med Choice™
Vision Care

Moxifloxacin

Moxidin®

5 mg/mL 0.5% w/v

Ophthalmic Solution
ANTIINFECTIVE (FLUOROQUINOLONE)
FOR EXTERNAL USE ONLY

℞

FORMULATION:
Each mL contains:
Moxifloxacin (as hydrochloride), EP.....5 mg

PRODUCT DESCRIPTION:
Pale green-yellow solution in a transparent plastic bottle.

INDICATIONS:
The treatment of bacterial conjunctivitis, tarsadenitis, keratitis (including corneal ulcer), caused by susceptible strains of the following organisms, aseptic therapy after ophthalmic surgery: *Staphylococcus aureus, Streptococcus, Streptococcus pneumoniae, Enterococcus, Micrococcus, Moraxella, Corynebacterium, Citrobacter, Klebsiella, Enterobacter, Serratia, Proteus, Morganella morganii, Haemophilus influenzae, Pseudomonas, Burkholderia cepacia, Stenotrophomonas maltophilia, Acinetobacter.*

DOSAGE AND ADMINISTRATION:
Bacterial conjunctivitis, tarsadenitis, keratitis (including corneal ulcer): 1 drop, three times a day. To increase or decrease, depending on the symptoms: redness of the eye, burning, itching, foreign body sensation, or mild pain or discomfort in the eye, thick sticky discharge from the eye, swollen and/or redness eyelids, sensitivity to light, blurred vision, decrease in vision.

Pharmacokinetic properties
No pharmacokinetic studies have been conducted with Moxidin. However, PK of its active, moxifloxacin hydrochloride can be confirmed by the studies as follows: Moxifloxacin was absorbed into the systemic circulation. Plasma concentration of moxifloxacin were measured in 21 male and female adult subjects who received bilateral topical ocular doses of moxifloxacin hydrochloride every 8 hours for a total of 13 doses. The mean steady-state Cmax and AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours. Moxifloxacin is widely distributed in the body and is excreted in feces or urine either unchanged or as glucuronide or sulfate conjugates.

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 gonorrheae	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 microorganisms: *Neisseria gonorrhoeae*; Other microorganisms: None
Inherently resistant organisms: Aerobic Gram-negative micro-organisms: *Pseudomonas aeruginosa*; Other microorganisms: None

1) Carcinogenicity: Although there have been no long-term animal studies conducted to determine carcinogenicity of this drug product, accelerated studies with cancer inducers and promoters have shown that there was no carcinogenicity when rats were orally dosed at 500 mg/kg/day for 38 weeks (about 21,700 times of the maximum recommended daily dose of ophthalmic use in humans).

2) Mutagenicity: There was no mutagenicity in the back mutation test using microorganisms. Like other quinolone drugs, TA 102 strains showed positive response by inhibiting DNA gyrase. Chromosomal aberration using CHO/HGPRT mammalian culture cells showed negative results. The same experiment was performed on v79 cells and the results were not clear. Chromosome induction was observed in the v79 chromosomal aberration test, but it was negative from the random DNA synthesis test using rat hepatocytes and the micronucleus test or dominant lethal test using mouse.

3) Fertility: There was no effect on fertility when administered orally at 500 mg/kg/day (about 21,700 times the maximum recommended amount per day for humans). However, the oral 500 mg/kg/day dose had a slight effect on the sperm morphology of male rats (separation of sperm head) and the estrous cycle of female rats.

4) There was no teratogenic effect when administered orally at 500 mg/kg/day (approximately 21,700 times the maximum recommended amount per day for ophthalmic use in humans) in pregnant rats in organogenesis. Minor developmental delays have been observed.

5) When fertilized cynomolgous monkeys were orally dosed at 100 mg/kg/day (about 4,300 times of the maximum recommended daily dose for ophthalmic use in humans who weigh 50 kg), there was no increase in teratogenicity.

PRECAUTIONS FOR USE
Warnings
Do not administer this drug product subconjunctivally or directly on anterior chamber of the eyes. In patients receiving quinolones, including any ingredients of this drug product, in a systemic administration routes, it has been reported to occur severe or fatal hypersensitivity in some after administering this product for one time. The following symptoms have also accompanied: Cardiovascular collapse, loss of consciousness, angioedema (including pharynx, larynx, and facial edema), airway obstruction, shortness of breath, hives, itching and the like.

Contraindications
For patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication; and for infants under 1 year old. Carefully administer to pregnant or lactating women.

ADVERSE DRUG REACTIONS:
Eye : conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, eye pain, itching, conjunctival hemorrhage and tears occurred in 1-6% of patients. Other: fever, cough, infection, otitis media, pharyngitis, rash, and rhinitis occurred in 1-4% of patients. According to pre-approval clinical trial perfomed in Japan, 32 cases (5.5%) of adverse events were reported in 586 patients. The most frequently reported adverse reactions were 18 cases of eye pain (3.1%), 8 cases of taste disorders (1.4%), 3 cases of eye redness, and 2 cases of eye irritation (0.3%). The study included 42 infants, and children (41 days of age or older). Two cases (4.8%) of eye pain, one case of taste disorder (2.4%), and three cases (7.1%) of adverse reactions were reported.

Serious adverse reactions
Shock or anaphylaxis : Since there have been reports of shock and anaphylaxis symptoms when taken orally, the symptoms must be observed sufficiently. In case of erythema, rash, dyspnea, reduced blood pressure, bleeding, edema and the like, suspend the administration and take appropriate measurements.

Other adverse reactions
In case of the following symptoms or adverse reactions, take appropriate measurements, such as suspension of the treatments.

	1% or more, 5% or less	*1% or more, 1% or less*
Eyes	*ocular pain*	*ocular hyperemia, irritation, keratitis*
		foreign body, eyelid edema, blurred vision
Others	*dysgeusia*	*paresthesia on the administration site*

The following includes adverse reactions that were reported in post-marketing experiences, but impossible to measure their frequency of occurrence (not known).
Heart : atrial fibrillation; *Nervous system*: dizziness; Eyes: endophthalmitis, ulcerative keratitis, corneal erosion, corneal abrasion, increased intraocular pressure, corneal opacity, corneal infiltration, allergies, keratitis, corneal edema, photophobia, corneal disorders, blepharitis, eyelid edema, tear production increased, ocular discharge, ocular discomfort; *Respiratory*: dyspnea; *Digestive System*: nausea; *Skin and subcutaneous tissue:* erythema, rash, itching; *Immune System*: hypersensitivity.

Reports of domestic post-marketing experiences
According to the post-marketing survey of 768 people for 6 years in Korea, the incidence of adverse reactions was 2.47% (19/768, 21 cases) regardless of causal relationship with this drug product. The incident of adverse drug reactions that cannot exclude their casual relationship with the drug was 2.21% (17/768, 19 cases). In terms of adverse drug reaction, ocular irritation occured most frequently(10/768, 10 cases), and the next came keratitis 0.39% (3/768, 3 cases), and 0.26% (2.768, 2 cases) of ocular discomfort, red eyes, and ocular pain respectively.

GENERAL PRECAUTIONS
When administering this drug product, identify sensitivity in order to prevent any occurrence of resistant bacteria and the like, and administer the product for the minimum period of time required for the treatment.
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. If any signs or symptoms of bacterial conjunctivitis appear, avoid wearing contact lenses. Systemic administration of quinolones, including any ingredients of this product, has been reported to induce hypersensitivity even after a single use. If any initial signs or symptoms of flare or allergic reactions, stop using this product immediately, and consult with your physician. This drug product should not be used for prevention or experimental treatments of gonococcal conjunctivitis, including gonorrheal ophthalmia in infants, caused by gonococci that is easily found to be resistant to quinolones. Patients with eye infections by gonococci must take appropriate systemic treatments. This drug product has not been evaluated in patients with eye infections by *Chlamydia trachomatis* who are 2 years old or younger. Thus, it is not recommended to use this product for the treatment of Chlamydia trachomatis eye infections. Patients who are 2 years old or older with eye infections caused by *Chlamydia trachomatis* also require appropriate systemic treatments.

DRUG INTERACTIONS
Drug-drug interaction studies have not been conducted with this drug. 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.

Use in Special Populations
Pregnancy: Since there are no adequate and well-controlled studies in pregnant women, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. *Lactating mothers*: Although moxifloxacin can be presumed to be excreted in human milk, caution should be exercised when it is administered to a nursing mother. *Pediatric use*: The safety and effectiveness of this drug in infants below 1 year 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 *Geriatric use*: No dosage adjustment necessary. There has been no difference between the aged and young adults in terms of safety and efficacy. *Use in hepatic and renal impairement:* Use in hepatic and renal impairment. *Females and males reporductive potential*: Studies have not been performed to evaluate the effect of ocular administration of Moxidin on human fertility.

PRECAUTIONS FOR ADMINISTRATION
Use it only for ophthalmic purposes. When administering this product, be careful not to contaminate the nozzle of the product with the eyes, fingers, or other materials. In order to prevent any contamination, do not share this product with others. In case of co-administration with other products, instill the products after having at least 5-minutes of interval.

OVERDOSAGE AND TREATMENT
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.

STORAGE
Store at temperatures not exceeding 30℃.
Keep out of reach of children. Preserve in tight container and avoid it from direct light.
To prevent misuse and preserve the quality of the product, do not transfer the solution to a different container.

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL
Any unused product or waste material should be disposed in accordance with local requirements.

AVAILABILITY
LDPE bottle with HDPE cap (Box of 1's)

SHELF-LIFE
24 months from the manufacturing date

CAUTION STATEMENT
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction."

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