For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

Senzmox®

Eye Drops 5ml

(Moxifloxacin Eye Drops IP 0.5% w/v)

COMPOSITION:

Moxifloxacin Hydrochloride IP equivalent to Moxifloxacin ..... 0.5% w/v
Water for injections IP ..... q.s.

Pharmacodynamic properties

Moxifloxacin is a fourth-generation fluoroquinolone antibacterial agent active against a broad spectrum of Gram-positive and Gram-negative ocular pathogens, atypical microorganisms and anaerobes.

Mechanisms of Action:

Moxifloxacin has in vitro activity against a wide range of Gram-positive and Gram-negative microorganisms. 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.

Mechanism(s) of Resistance:

In vitro resistance to moxifloxacin develops slowly via multiple-step mutations and occurs at a general frequency between 10-9 to 10-11 for Gram-positive bacteria.

Fluoroquinolones, including moxifloxacin, differ in chemical structure and mode of action from beta-lactamantibiotics, macrolides and aminoglycosides, and therefore may be active against bacteria resistant to beta-lactam antibiotics, macrolides and aminoglycosides.

Breakpoints There are no official topical ophthalmic breakpoints for moxifloxacin and although systemic breakpoints have been used, their relevance to topicalophthalmic therapy is doubtful. The systemic breakpoint used for this antibiotic is S<2mg/L, R>4mg/L.

Pharmacokinetics:

Plasma concentrations of moxifloxacion were measured in healthy adult male and female subjects who received bilateral topical ocular doses of Moxifloxacin 3 times a day. The mean steady-state Cmax (2.7 ng/mL) and estimated daily exposure AUC (45 ng.hr/mL) values were 1,600 and 1000 times lower than the mean Cmax and AUC reported after therapeutic 400 mg oral doses ofmoxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

Microbiology:

Moxifloxacin is an 8-methoxy fluoroquinolone with a diazabicyccloononyl ring at the C7 position. 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 X 10-9 to < 1 X 10-11 for Grampositive 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: Moxifloxacin solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains ofthe following organisms.

Inductions:

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

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

Anaerobic microorganisms :
Clostridium perfringens
Fusobacterium species
Prevotella species
Propionibacterium acnes

Other microorganisms :
Chlamydia pneumoniae
Legionella pneumophila
Mycobacterium avium
Mycobacterium marinum
Mycoplasma pneumoniae

Aerobic Gram-negative microorganisms :
Acinetobacter lwoffii
Haemophilus influenzae
Haemophilus parainfluenzae

Other microorganisms :
Chlamydia trachomatis

AerobicGram-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

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

Contraindications: Senzmox is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication

Clinical Studies:

In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, moxifloxacin solution produced clinical cures on day 5-6 in 66% to 69% of patients treated for bacterial conjunctivitis. Microbiological success rates for the eradication of the baseline pathogens ranged from 84% to 94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

Warnings: NOT FOR INJECTION.

Senzmox should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye. In patients receiving systematically 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.

Precautions:

General: As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible 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. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source. Systematically administered quinolones including moxifloxacin have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions : Drug interaction studies have not been conducted with MOXIFLOXACIN@ solution. In vitro studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYPIA2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility : Long-term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed.

However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose for a 50 Kg person, on a mg/kg basis).

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 assaywhen v 79 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 21,700 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 he estrous cycle in female rats.

Pregnancy: Teratogenic Effects.

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 Senzmox is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of Senzmox in infants below I 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

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

Adverse Reactions:

The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocularpain, ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% ofpatients.

Nonocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash and rhinitis.

Dosage and Administration: Instill one drop in the affected eye 3 times a day for 7 day

Storage and handling instructions:

Keep in cool place

Use the solution within one month after opening the container.

Do not touch the tip of the container to any surface. Replace cap after using. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

NOT FOR INJECTION

FOR EXTERNAL USE ONLY

Presentation:

Senzmox is a sterile solution supplied in opaque plastic dropper bottle with a cap, Containing 5 ml of the solution.

Directions for use :

Turn the tamper proof cap anti-clockwise to break the seal.

Remove the cap, dispense drops with gentle pressure.

Replace the cap immediately after every use.

Manufactured in INDIA by :

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