LEOS®-MX

Eye Drops

(Moxifloxacin 0.5% w/v with Loteprednol Etabonate 0.5% w/v Ophthalmic Suspension)

COMPOSITION:

Moxifloxacin Hydrochloride IP Eq. to Moxifloxacin……..... 0.5% w/v
Loteprednol Etabonate …..... 0.5% w/v
Benzalkonium Chloride Solution IP…..... 0.01% v/v
(As preservative)
Water for injections IP…..... q.s.

Description

Leos-MX is a combination of Moxifloxacin a fluoroquinolone antimicrobial and Loteprednol Etabonate an anti-inflammatory corticosteroid.

Moxifloxacin: Moxifloxacin is an 8-methoxy fluoroquinolone with a diazabicyclononyl ring at the C7 position. The antibacterial action of Moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV.

Loteprednol Etabonate: Loteprednol Etabonate is structurally similar to other corticosteroids. However the number 20 position ketone group is absent. It is highly lipid soluble which enhances its penetration into cells. Loteprednol Etabonate is synthesized through structural modifications of prednisolone-related compounds so that it will undergo a predictable transformation to an inactive metabolite.

Corticosteroids suppress the inflammatory response to a variety of agents and they probably delay or slow healing.

Since corticosteroids may inhibit the body's defense mechanism against infection, a concomitant antimicrobial drug may be used when this inhibition is considered to be clinically significant.

Clinical Pharmacology

Mechanism of Action

Moxifloxacin: 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 the 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, aminogylcosides 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 systematic Moxifloxacin and some other quinolones

Loteprednol Etabonate: Corticosteroids inhibit the inflammatory response to a variety of inciting agents and probably dealing or no slow healing. They inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, fibroblast proliferation, deposition of collagen and scar formation associated with inflammation. There is no generally accepted explanation for the mechanism of action of ocular corticosteroids. However corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2. Corticosteroids are capable of producing a rise in intraocular pressure.

Loteprednol Etabonate is structurally similar to other corticosteroids. However the number 20 position ketone group is absent. It is highly lipid soluble which enhances its penetration in to the cells. Loteprednol Etabonate is synthesized through structural modification of prednisolone related compounds so that it will undergo a predictable transformation to an inactive metabolite. Based upon in vivo preclinical metabolism studies, Loteprednol Etabonate undergoes extensive metabolism to inactive carboxylic acid metabolites.

Clinical studies

Moxifloxacin: In two randomized double masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days. Moxifloxacin Eye Drops 0.5 % w/v 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 pathogen ranged from 84% to 94%. Please note that microbiological eradication does not always correlate with clinical outcome in anti-infective trials.

Loteprednol Etabonate

Post-operative Inflammation: Placebo-controlled clinical studies demonstrated that Loteprednol Etabonate Ophthalmic Suspension 0.5% is effective for the treatment of anterior chamber inflammation as measured by the cell and flare

Giant Papillary Conjunctivitis: Placebo-controlled clinical studies demonstrated that Loteprednol Etabonate ophthalmic Suspension 0.5% was effective in reducing the signs and symptoms of giant papillary conjunctivitis after one week of treatment and continuing for up to six weeks while on treatment.

Seasonal Allergic Conjunctivitis: A Placebo-controlled clinical studies demonstrated that Loteprednol Etabonate ophthalmic Suspension 0.5% was effective in reducing the signs and symptoms of allergic conjunctivitis during peak periods of pollen exposure.

Uveitis: Controlled clinical studies of patients with uveitis demonstrated that Loteprednol Etabonate Ophthalmic Suspension 0.5% was effective than prednisolone acetate 1%. Overall 72% of patients treated Loteprednol Etabonate Ophthalmic Suspension 0.5% experienced resolution of anterior chamber cell by day 28, compared to 87% of patients treated with 1% prednisolone acetate. The incidence of patients with clinically significant increases in IOP ($\geq$ 10 mmHg) was 1% with Loteprednol Etabonate Ophthalmic Suspension 0.5% and 6% with prednisolone acetate 1%.

Indications and Usage

Leos-MX is indicated in the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms associated with steroid responsive inflammation.

Aerobic Gram-positive microorganisms: Cornyebacterium species *, Micrococcus luteus*, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus warneri*, Streptococcus pneumoniae, Streptococcus viridans group.

Aerobic Gram-negative microorganisms: Acinetobacter iwofii*, Haemophilus influenzae, Haemophilus parainfluenzae*.

Other microorganisms: Chlamydia trachomatis.

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

Dosage and Administration

The recommended dose of Leos-MX is one drop instilled in to the conjunctival sac of the affected eye(s) three times daily or as directed by the Physician.

Contraindications

Leos-MX is contraindicated with known or suspected hypersensitivity in any of the ingredients of this preparation and other corticosteroids.

Leos-MX is contraindicated in viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia and varicella and also mycobacterial infection of the eye and fungal diseases of ocular structures.

Precautions

General

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 a 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 the signs and symptoms of bacterial conjunctivitis. As with all ophthalmic preparations containing benzalkonium chloride, patients should be advised not to wear soft contact lenses when using Leos-MX.

If this product is used for 10 days or longer, intraocular pressure should be monitored even though it may be difficult in children and uncooperative patients

Fungal infections of the cornea are particularly prone to develop coincidentally with long term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

If pain develops, redness, itching or inflammation becomes aggravated; the patient should be advised to consult a physician.

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 teratogenecity 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 Eye Drops 0.5%w/v should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Loteprednol Etabonate: Teratogenic Effects: Pregnancy category C.

Loteprednol Etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic increased incidence of meningocele, abnormal left common carotid artery and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose) a dose which caused no maternal toxicity. The no-observed-effect-level

(NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose).

Nursing mothers

Moxifloxacin: 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 Eye Drops 0.5% w/v is administered to a nursing mother

Loteprednol Etabonate: It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systematic absorption to produce detectable quantities in human milk. Systematic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Loteprednol Etabonate Ophthalmic Suspension 0.5 %is administered to a nursing woman

Pediatric Use

The safety and effectiveness of Moxifloxacin Eye Drops 0.5% w/v in infants below one year of age has not been established

There is no evidence that the ophthalmic administration of Moxifloxacin Eye Drops 0.5% w/v has any effect on weight bearing joints even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Loteprednol Etabonate: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

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

Adverse Reactions

Moxifloxacin

The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage and tearing. These events occurred in approximately 1.6% of patients.

Nonocular adverse events reported at a rate of 1.4 % were fever, increased cough, infection, otitis media, pharyngitis, rash and rhinitis.

Loteprednol Etabonate: Reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

Overdosage: No information available.

Warnings

- Use the suspension within one month after opening the container.
- If irritation persists or increases, discontinue the use and consult the physician.
- Do not touch the dropper tip or other dispensing tip to any surface since this may contaminate suspension
- If the suspension becomes dark brown, it should be discarded.
- Indiscriminate and prolonged use of the preparation may lead to glaucoma, cataract and fungal infections
- 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, lose of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction; dyspnea, urticaria and itching. If an allergic reaction to Moxifloxacin occurs, discontinue the use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Storage : Keep in a cool place, Protect from light.

KEEP OUT OF REACH OF CHILDREN

NOT FOR INJECTION

FOR EXTERNAL USE ONLY

SHAKE WELL BEFORE USE

Presentation: Leos-MX is a sterile ophthalmic suspension supplied in opaque plastic dropper bottle with a cap, Containing 5 ml of the suspension.

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 :

Senses Pharmaceuticals Pvt. Ltd.,

No.77, 3rd Road, Bommasandra Industrial Area,
Bommasandra 4th Phase, Bengaluru - 560 099.

MLEPI-04

Month of publication of pack insert: January 2022