dexamethasone therapy. 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 monkey was given oral doses as high as 100 mg/kg/day (approximately 4300 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, MYTICOM™ solution should be used during pregnancy only if the potential benefit justifies the potential risk to fetus.

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Many drugs are excreted in human milk, thus caution should be exercised when MYTICOM™ ophthalmic solution is administered to a nursing mother.

USE IN CHILDREN
Safety and effectiveness in pediatric patients have not been established.

USE IN THE ELDERLY
No changes of dose are required for elderly patients.

UNDESIRABLE EFFECTS
The adverse reactions that may occur with use of corticosteroids are: Glaucoma with optic nerve damage, visual acuity defects and visual field defects; cataract formation; secondary ocular infection following suppression of host response; and perforation of the globe. The most frequently ocular adverse reported with the use of moxifloxacin ophthalmic solution 0.5% were conjunctivitis, decreased visual acuity, dry eye, keratitis; ocular discomfort, ocular hyperemia, ocular pain and ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% of patients. In surgical procedures, some of these events are consequence of the surgery. Non-ocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash and rhinitis.

DRUG INTERACTIONS
Drug-drug interaction studies have not been conducted with MYTICOM™ 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. Based on findings from systemic administration studies, corticosteroids may increase the activity of barbiturates, tricyclic antidepressants and decrease the activity of anticholinesterase agents, salicylates and anticoagulants. The relevance of these observations for the ophthalmic administration has not been studied.

STORAGE INSTRUCTIONS
Store in a cool place. Protect from light.

Marketed by
ALLERGAN INDIA PRIVATE LIMITED

Manufactured in India by :
Piramal Enterprises Limited
Plot No. 67-70, Sector 2, Pithampur-454 775,
Dist. Dhar, Madhya Pradesh.

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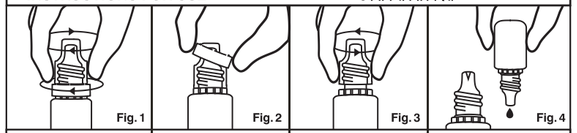
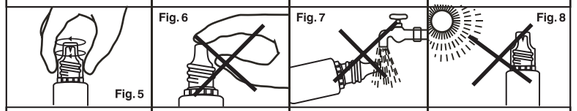
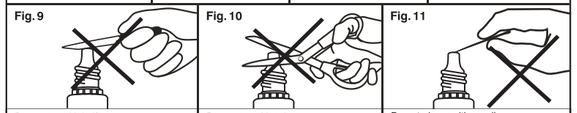
INSTRUCTIONS FOR USE — उपयोग संबंधी निर्देश



Turn right (clockwise) to break the seal and make a dispensing hole on the nozzle	Remove the ring and discard	Open the cap by turning left (anti-clockwise) and it is ready for use.	Turn it up side down. Squeeze the walls of the bottle gently to deliver sterile drop into the eye.
सिल तोड़ने एवम नोज़ल में छिद्र करने के लिये ढक्कन को दाहने तरफ घुमायें।	छल्ले को नीकाल कर फेंक दें।	ढक्कन को खोलने के लिये बांयी तरफ घुमायें। अब बोतल उपयोग के लिये तैयार है।	अब बोतल को उल्टा करें, बोतल की दिवार को हलकेसे दबाएँ और आँखों में दवा की बूंदें डालें।



Replace the cap. Tighten it firmly and keep the bottle closed for subsequent use.	Do not touch the dropper.	Do not rinse the dropper.	Do not expose to Sunlight.
पुनः उपयोग में लाने तक ढक्कन को कसकर बोतल बाध्य बंद कर दें।	बोतल के नोज़ल को हाथ न लगाएँ।	नोज़ल को कभी न धोएँ।	बोतल को धूप में न रखें।



Do not cut with knife	Do not cut with scissor	Do not pierce with needle
चाकु से ना काटें।	कैची से ना काटें।	सुई से छिद्र न करें।

State of the art technology
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अलरगन इंडिया प्राईवेट लिमिटेड द्वारा

A33/d

For The Use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Moxifloxacin and Dexamethasone Eye Drops

MytiCom™ Allergan™

Composition :

Moxifloxacin Hydrochloride IP equivalent to Moxifloxacin	0.5% w/v
Dexamethasone Phosphate	0.1% w/v
Benzalkonium chloride solution (As preservative) IP	0.02% w/v
Sterile Aqueous buffered vehicle	q.s.

DESCRIPTION
MYTICOM™ is a sterile, isotonic ophthalmic solution which combines moxifloxacin hydrochloride and dexamethasone sodium phosphate. Patients that may benefit from the topical combined therapy with an antibiotic agent and an anti-inflammatory agent include patients that have been submitted to ocular surgery eg, cataract extraction and refractive surgery. The instillation of a combination steroid and antibiotic is beneficial to these patients in the following ways: The steroid suppresses the inflammation while the antibiotic controls the proliferation of potential susceptible pathogenic bacteria and also works prophylactically.

INDICATION
Moxifloxacin and Dexamethasone Eye Drops is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial ocular infection exists. The combination can also be used for post-operative inflammation and any other ocular inflammation associated with infection.

MECHANISM OF ACTION
MYTICOM™ sterile ophthalmic solution contains the antibiotic moxifloxacin hydrochloride, which destroys the susceptible bacteria that cause ocular infection, and the anti-inflammatory dexamethasone phosphate (steroid).

PHARMACODYNAMICS
The mechanism of action of moxifloxacin (and other fluoroquinolone antimicrobials) involves the inhibition of bacterial topoisomerase IV and deoxyribonucleic acid (DNA) gyrase enzymes required for DNA replication, transcription, repair, and recombination. In gram-negative bacteria, fluoroquinolones preferentially target DNA gyrase rather than topoisomerase IV. Whereas in gram-positive bacteria, the target specificity is reversed.

Moxifloxacin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections. Aerobic Gram-Positive Microorganism: Corynebacteriumsp*, Micrococcus luteus*, Staphylococcus aureus,

Staphylococcus epidermidis, Staphylococcus haemolyticus,Staphylococcus hominis, Staphylococcus warneri*, Streptococcus pneumoniae e Grupo dos Streptococcus viridans.

Aerobic Gram-Negative Microorganisms: Acinetobacter Iwoffii*, Haemophilus influenzae, Haemophilus parainfluenzae*.

*Efficacy for this organism was studied in fewer than 10 patients with infection.

Corticosteroids achieve their anti-inflammatory effects though decreased release of arachidonic acid as well as suppression of vascular endothelial cell adhesion molecules, cyclooxygenase and cytokine expression. This action results in a reduced release of pro-inflammatory mediators and reduced adhesion of circulating leukocytes to vascular endothelium, preventing their passage into inflamed ocular tissue. Additionally, decreased expression of cyclooxygenase results in a decreased production of inflammatory prostaglandins, which are known to cause breakdown of the blood aqueous barrier and leakage of plasma proteins into the ocular tissue.

Efficacy Results: In 2 randomized, double-masked, multicenter, controlled, clinical trials in which patients were dosed 3 times a day for 4 days, the solution of moxifloxacin 0.5% produced clinical cures on days 5-6 in 66-69% of patients treated for bacterial conjunctivitis. Microbial success rates for the eradication of base pathogens ranged from 84-94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials. In 2 randomized, double-masked clinical trials in which patients were dosed 4 times/day with Moxifloxacin 0.5% +Dexamethasone 0.3% sterile ophthalmic solution, starting the treatment 1 day before the surgery and during 2 weeks after the surgery, no patients developed ocular infection.

PHARMACOKINETICS
Plasma concentrations of moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of ophthalmic solution of moxifloxacin 0.5% 3 times a day. The mean steady-state Cmax (2.7 ng/mL) and estimated daily exposure AUC (45 ng·hr/mL) values were 1600 and 1000 times lower than the mean Cmax and AUC reported after therapeutic oral doses of moxifloxacin 400 mg. The plasma half-life of moxifloxacin was estimated to be 13 hrs. Dexamethasone phosphate is rapidly converted to dexamethasone in humans. Following topical administration of a single drop of ophthalmic solution of dexamethasone 0.1% in patients undergoing cataract surgery, aqueous humor levels of dexamethasone at 90-120 min post-dose average 31 ± 3.9 ng/mL.

DOSAGE & ADMINISTRATION
Prevention of Post-Surgery Ocular Inflammation and Infection: Instill 1 drop, 4 times/day in the eye to be operated, starting 1 day before the surgery and during 15 days after the surgery.

Treatment of Ocular Infections Caused by Susceptible Organisms: Instill 1 drop 4 times / day during 7 days, or as directed by the doctor.
Do not use outdated medicine. Observe the appearance of the medicine before using it.
Patients Submitted to Cataract Surgery: Instill the solution immediately after the surgery.
Patients Submitted to Refractive Surgery by LASIK: Instill the solution within 15 min after the surgery.

Administration: To prevent contaminating the dropper tip and solution, care should be taken not to touch any surface with the dropper tip of the bottle. Doctor's instructions on the schedule, dose and duration of treatment should be followed. Do not discontinue treatment without consulting the doctor.

OVERDOSAGE
In case of excessive instillation in the eye, rinse with sufficient warm water. Do not instill the product again until the time of the next dose.

CONTRAINDICATIONS
Moxifloxacin and Dexamethasone Eye Drops is contraindicated in epithelial herpes simplex keratitis (Dendritic keratitis), vaccinia, varicella, and in many other viral diseases of the conjunctiva and cornea, Mycobacterial infection of the eye and fungal diseases of ocular structures and in individuals hypersensitive to any of the components of the medication.

WARNINGS
If an allergic reaction to moxifloxacin occurs, discontinue use of MYTICOM™ and contact the doctor. Prolonged steroid use may result in ocular hypertension and/or glaucoma with damage to the optic nerve, defect in visual acuity and fields of vision, posterior subcapsular cataract formation, or increased hazard of developing secondary ocular infections. The intraocular pressure must be evaluated routinely. In those diseases causing thinning of the cornea or sclera (white part of the eye), perforations have been known to occur with use of topical corticosteroids. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

NOT FOR INJECTION

MYTICOM™ solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye. In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the 1st dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria and itching. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

SPECIAL PRECAUTIONS
General: As with other antibiotic preparations, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated. Whenever clinical judgment dictates, the patient should be examined by biomicroscopy and, where appropriate, fluorescein staining. The possibility of fungal infections of the cornea should be considered after long-term steroid dosing.

CARCINOGENICITY, MUTAGENICITY & IMPAIRMENT OF FERTILITY
Long-term studies in animals to determine the carcinogenic potential of dexamethasone sodium phosphate and 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 500 mg/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 4 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 21,700 times the highest recommended total day 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.

USE IN PREGNANCY & LACTATION
Corticosteroids have been found to be teratogenic in animal studies. Ocular administration of dexamethasone 0.1% resulted in 15.6% and 32.3% incidence of fetal anomalies in 2 groups of pregnant rabbits. Fetal growth retardation and increased mortality rates have been observed in rats with chronic