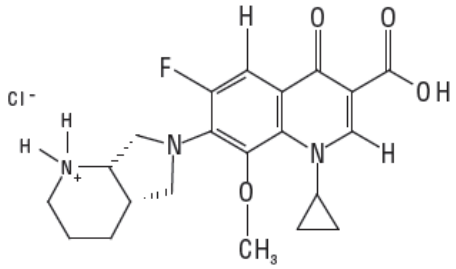
1. NAME OF THE MEDICINAL PRODUCT

VIGAMOX®

5 mg/ml eye drops, solution

(moxifloxacin hydrochloride ophthalmic solution)

VIGAMOX® (moxifloxacin HCl ophthalmic solution) 0.5% is a sterile ophthalmic solution. It is an 8-methoxy fluoroquinolone anti-infective for topical ophthalmic use.



$C_{21}H_{24}FN_3O_4 \bullet HCl$ Mol Wt 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.

Moxifloxacin hydrochloride is a slightly yellow to yellow crystalline powder.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of VIGAMOX solution contains 5.45 mg moxifloxacin hydrochloride equivalent to 5 mg moxifloxacin base.

VIGAMOX solution is an isotonic solution with an osmolality of approximately 290 mOsm/kg.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye drops (solution)

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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-negative microorganisms:
*Acinetobacter lwoffii**
Haemophilus influenzae
*Haemophilus parainfluenzae**

Other microorganisms:
Chlamydia trachomatis

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

Pediatric Use: The safety and effectiveness of VIGAMOX solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of VIGAMOX solution 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 overall differences in safety and effectiveness have been observed between elderly and younger patients.

4.2 Posology and method of administration

Instill one drop in the affected eye 3 times a day for 7 days.

4.3 Contraindications

Hypersensitivity to the active substance, to other quinolones or to any of the excipients.

4.4 Special warnings and precautions for use

• For ocular use only. Not for injection. VIGAMOX solution should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye.

• In patients receiving systemically administered quinolones, 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 oedema), airway obstruction, dyspnoea, urticaria, and itching.

• If an allergic reaction to VIGAMOX solution occurs, discontinue use of the product. Serious acute hypersensitivity reactions to moxifloxacin may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated.

• 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.

• Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including moxifloxacin, particularly in elderly patients and in those treated concurrently with corticosteroids. Therefore, treatment with VIGAMOX solution should be discontinued at the first sign of tendon inflammation.

• 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.

Systemically 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.

4.5. Interaction with other medicinal products and other forms of interaction

Given the low systemic concentration of moxifloxacin following topical ocular administration of the medicinal product, drug interactions are unlikely to occur.

4.6 Fertility, pregnancy and lactation

Fertility

Studies have not been performed to evaluate the effect of ocular administration of VIGAMOX solution on fertility.

Pregnancy

Teratogenic Effects.

Pregnancy Category C

There are no or limited amount of data from the use of [Moxifloxacin Eye Drops, Solution] in pregnant women. However, no effects on pregnancy are anticipated since the systemic exposure to moxifloxacin from topical ocular application is negligible

Breast-feeding

It is unknown whether moxifloxacin / metabolites are excreted in human milk. Animal studies have shown excretion of low levels in breast milk after oral administration of moxifloxacin. However, at therapeutic doses of VIGAMOX solution no effects on the suckling child are anticipated.

4.7 Effects on ability to drive and use machines

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at application, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

The following adverse reactions have been reported during clinical trials with [Moxifloxacin 5 mg/ml Eye Drops, Solution] and are classified according to the following convention:
very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	**Adverse reactions** *MedDRA Preferred Term (v.15.1)*
Blood and lymphatic system disorders	*Rare:* haemoglobin decreased
Nervous system disorders	*Uncommon:* headache *Rare:* paresthesia
Eye disorders	*Common:* eye pain, eye irritation

	Uncommon: punctate keratitis, dry eye, conjunctival haemorrhage, ocular hyperaemia, eye pruritus, eyelid oedema, ocular discomfort *Rare*: corneal epithelium defect, corneal disorder, conjunctivitis, blepharitis, eye swelling, conjunctival oedema, vision blurred, visual acuity reduced, asthenopia, erythema of eyelid
Respiratory, thoracic and mediastinal disorders	*Rare*: nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat)
Gastrointestional disorders	*Uncommon*: dysgeusia *Rare*: vomiting
Hepatobiliary disorders	*Rare:* alanine aminotransferase increased, gammaglutamyltransferase increased

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

Additional adverse reactions identified from post-marketing surveillance include the following. Frequencies cannot be estimated from the available data. Within each system Organ Class adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	**Adverse reactions** *MedDRA Preferred Term (v.15.1)*
Immune system disorders	hypersensitivity
Nervous system disorders	dizziness
Eye disorders	ulcerative keratitis, keratitis, lacrimation increased, photophobia, eye discharge
Cardiac disorders	palpitations
Respiratory, thoracic and mediastinal disorders	dyspnoea
Gastrointestional disorders	nausea
Skin and subcutaneous tissue disorders	erythema, pruritus, rash, urticaria

4.9 Overdose

Due to the characteristics of this preparation no toxic effects are to be expected with an ocular overdose of the product, or in the event of accidental ingestion of the contents of one bottle.

5. PHARMACOLOGICAL PROPERTIES

Pharmacokinetics properties

Plasma concentrations of moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of VIGAMOX solution 3 times a day. The mean steady-state C_{max} (2.7 ng/mL) and estimated daily exposure AUC (45 ng·hr/mL) values were 1,600 and 1,000 times lower than the mean C_{max} and AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

Microbiology:

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. 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 1.8×10^{-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 section 4.1:

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-negative microorganisms:

*Acinetobacter lwoffii**

Haemophilus influenzae
*Haemophilus parainfluenzae**

Other microorganisms:
Chlamydia trachomatis

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

The following *in vitro* data are also available, **but their clinical significance in ophthalmic infections is unknown.** The safety and effectiveness of VIGAMOX solution in treating ophthalmological infections due to these microorganisms have not been established in adequate and well-controlled trials.

The following organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the *in vitro* systemic breakpoint and ophthalmological 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 2µg/mL or less (systemic susceptible breakpoint) against most (≥90%) of strains of the following ocular pathogens.

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

Aerobic Gram-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

Pseudomonas stutzeri

Anaerobic microorganisms:
Clostridium perfringens
Fusobacterium species
Prevotella species
Propionibacterium acnes

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

Clinical Studies:
In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, VIGAMOX 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Boric acid, sodium chloride, and purified water. May also contain hydrochloric acid/sodium hydroxide to adjust pH to approximately 6.8.

6.2 Incompatibilities
Not applicable

6.3 Special precautions for storage
Do not store above 30 °C

6.4 Nature and content of container

VIGAMOX (moxifloxacin hydrochloride ophthalmic solution) 0.5% is supplied as a sterile ophthalmic solution in Alcon's DROPTAINER dispensing system consisting of a natural low density polyethylene bottle and dispensing plug and white polypropylene closure. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

1.5 ml, 3ml, 5ml
Not all presentations are available locally.

6.5 Special precautions for disposal

No special requirement

6.6 Manufacturer

Refer to folding box

Rx Only

(Information Issued: April 2013.SINv1)

Novartis Pharma AG, Basel, Switzerland