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

Ketorolac Tromethamine and
Moxifloxacin Ophthalmic Solution 0.5 % w/v & 0.5 % w/v

SENZMOX®-KT

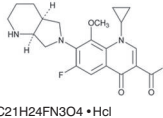
For the use of Registered Medical Practitioner only

Composition

Ketorolac Tromethamine USP ..... 0.5% w/v
Moxifloxacin Hydrochloride USP equivalent to Moxifloxacin ..... 0.5% w/v
Benzalkonium Chloride Solution USP ..... 0.02% v/v
(as preservative)
Water for Injection USP ..... q.s

Chemical Structure & Name

Moxifloxacin Hydrochloride

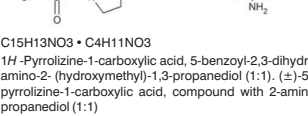


C21H24FN3O4 • Hcl

(4a*S* -*cis*)-1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(octahydro-6*H* -pyrrolo[3,4-*b*]pyridin-6-yl)-4-oxo-3-quinolinecarboxylic acid, monohydrochloride.

1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*S* ,7a*S*)-octahydro-6*H* -pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride

Ketorolac Tromethamine



C15H13NO3 • C4H11NO3

1*H* -Pyrrolizine-1-carboxylic acid, 5-benzoyl-2,3-dihydro, (±)-, compound with 2-amino-2- (hydroxymethyl)-1,3-propanediol (1:1). (±)-5-Benzoyl-2,3-dihydro-1*H* -pyrrolizine-1-carboxylic acid, compound with 2-amino-2- (hydroxymethyl)-1,3-propanediol (1:1)

Description

A clear, greenish yellow colored solution filled in 5mL Sterile Gamma-irradiated white opaque LDPE bottle sealed with Sterile Gamma-irradiated natural transparent LDPE open nozzle and Sterile Gamma-irradiated white HDPE tamp safe cap

Pharmacology

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. 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 crossresistance between moxifloxacin and the aforementioned classes of antibiotics. Cross resistance has been observed between systemic moxifloxacin and some other quinolones.

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:

Corynebacteriumspecies including

Corynebacteriumdiphtheriae

Micrococcus luteus

Staphylococcus aureus

Staphylococcus epidermidis

Staphylococcus haemolyticus

Staphylococcus hominis

Staphylococcus warneri

Streptococcus pneumoniae

Streptococcus viridansgroup

Aerobic Gram-negative micro-organisms:

Acinetobacterlwoffii

Haemophilusinfluenzae

Haemophilusparainfluenzae

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 micro-organisms:

Neisseria gonorrhoeae

Other micro-organisms:

None

INHERENTLY RESISTANT ORGANISMS

Aerobic Gram-negative micro-organisms:

Pseudomonas aeruginosa

Other micro-organisms:

None

Ketorolac tromethamine

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug which, when administered systemically, has demonstrated analgesic, anti-inflammatory, and antipyretic activity. The mechanism of its action is thought to be due to its ability to inhibit prostaglandin biosynthesis. Prostaglandins have been shown in many animal models to be mediators of certain kinds of intraocular inflammation. In studies performed in animal eyes, prostaglandins have been shown to produce disruption of the blood aqueous humor barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.

Prostaglandins also appear to play a role in the miotic response produced during ocular surgery by constricting the iris sphincter independently of cholinergic mechanisms. Ocular administration of ketorolac tromethamine reduces prostaglandin E2 (PGE2) levels in aqueous humor.

Results from clinical studies indicate that ketorolac tromethamine has no significant effect on intraocular pressure.

Pharmacokinetic:

Moxifloxacin

Following topical ocular administration of Moxifloxacin, Moxifloxacin was absorbed into the systemic circulation. Plasma concentrations of moxifloxacin were measured in 21 male and female subjects who received bilateral topical ocular doses of the medicinal product 3 times a day for 4 days. The mean steady-state Cmaxand AUC were 2.7 ng/ml and 41.9 ng•hr/mL, respectively. These exposure values are approximately 1,600 and 1,200 times lower than the meanCmaxand AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours Ketorolac tromethamine

Two drops of 0.5% ketorolac tromethamine ophthalmic solution instilled into the eyes of patients 12 hours and 1 hour prior to cataract extraction achieved a mean ketorolac concentration of 95 ng/mL in the aqueous humor of 8 of 9 eyes tested (range 40 to 170 ng/mL).

One drop of 0.5% ketorolac tromethamine ophthalmic solution was instilled into 1 eye and 1 drop of vehicle into the other eye TID in 26 healthy subjects. Five (5) of 26 subjects had detectable concentrations of ketorolac in their plasma (range 11 to 23 ng/mL) at Day 10 during topical ocular treatment. The range of concentrations following TID dosing of 0.5% ketorolactromethamine ophthalmic solution are approximately 4 to 8% of the steady state mean minimum plasma concentration observed following four times daily oral administration of 10 mg ketorolac in humans (290 ± 70 ng/mL).

Indications

Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution is indicated for NSAIDresponsive inflammatory ocular conditions for which a NSAID is indicated and where bacterial infection or a risk of bacterial ocular infection exists. The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

Dosage & Administration

Instill one drop in the affected eye 3 times a day for 5 to 7 days.

Method of Administration:

For ocular use only.

Care should be taken not to discontinue the therapy prematurely.

Contraindications

Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, ketorolac or to any of the components in this medication.

The potential exists for cross sensitivity to acetylsalicylic acid and other nonsteroidalantiinflammatory drugs. Ketorolac is contraindicated in individuals who have previously exhibited sensitivities to these drugs.

Warning and Precaution

This product is for ocular use only.

Ketorolac Tromethamine and Moxifloxacin Ophthalmic 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 first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), 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.

As with other anti-infective, 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. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Data are very limited to establish efficacy and safety of moxifloxacin in the

treatment of conjunctivitis in neonates. Therefore, use of this medicinal product to treat conjunctivitis in neonates is not recommended. The medicinal product is not recommended for the treatment of Chlamydia trachomatis in patients less than 2 years of age as it has not been evaluated insuch patients. Patients older than 2 years of age with eye infections caused by Chlamydia trachomitisshould receive appropriate systemic treatment. Neonates with ophthalmianeonatorum should receive appropriate treatment for their condition, e.g. systemic treatment in cases caused by Chlamydia trachomitisor Neisseria gonorrhoeae.

Moxifloxacin should not be used for the prophylaxis or empiric treatment of gonococcal conjunctivitis, including gonococcalophthalmianeonatorum, becauseof the prevalence of fluoroquinolone resistant Neisseria gonorrhoeae. Patients with eye infections caused by Neisseria gonorrhoeaeshould receive appropriate systemic treatment.

All topical nonsteroidal anti-inflammatory drugs (NSAIDs) may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs. There have been reports of bronchospasm or exacerbation of asthma in patients with the use of ketorolac tromethamine in patients who have either a known hypersensitivity toaspirin/nonsteroidal anti-inflammatory drugs or a past medical history of asthma. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

In common with other anti-inflammatory drugs, ketorolac may mask the usual signs of infection.

With some NSAIDs, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

It is recommended that ketorolac should be used with caution in patients with known bleeding tendencies or who are receiving other medications, which may prolong bleeding time.

Concomitant use of ketorolac and topical corticosteroids should be exercised with caution in patients susceptible to corneal epithelial breakdown.

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs and should be closely monitored for corneal health.

Post marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Post marketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events when used either alone or in combination with antibiotics.

The preservative in of Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution 0.5 % w/v & 0.5 % w/v, benzalkonium chloride, may cause eye irritation. Contact lenses must be removed prior to application, with at least a 15-minute wait before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses. Contact with soft contact lenses must be avoided.

Paediatric Use

Safety and efficacy in paediatric patients below the age of 3 years have not been established.

Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution is not recommended in children below 3 years of age.

Geriatric Use

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

As with any eye drops, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient should wait until their vision clears before driving or using machinery.

Interactions

No interaction studies have been performed for Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution. Drug –drug interaction studies have not been conducted with moxifloxacin. 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 this cytochrome P450 isozymes.

Ketorolac has been safely administered with systemic and ophthalmic medications such as antibiotics, sedatives, beta blockers, carbonic anhydrase inhibitors, miotics, mydriatics, local anaesthetics and cycloplegics.

Pregnancy & Lactation

There are no adequate and well controlled studies in pregnant women. Hence, Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution ophthalmic solution should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Lactation

Caution should be exercised when Ketorolac Tromethamine and Moxifloxacin Ophthalmic Solution ophthalmic solution is administered to a nursing mother.

Adverse reaction

The most frequently reported ocular adverse events were burning on instillation, conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, transient stinging and tearing.

The following undesirable effects were assessed to be treatment related and from postmarketing experience 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 <1/1000), or very rare (<1/10,000) or not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Blood and Lymphatic System Disorders

Uncommon: haemoglobin decreased

Nervous System Disorders

Common: dysgeusia

Uncommon: headache, paraesthesia

Not known: dizziness

Eye Disorders

Very common: Eye irritation (including burning sensation), Eye pain (including stinging)

Common: Superficial (punctate) keratitis, eye and/or eyelid oedema, ocular pruritus, conjunctivalhyperaemia, eye infection, eye inflammation

Uncommon: Corneal epithelium defect, punctate keratitis, corneal staining, conjunctival haemorrhage, conjunctivitis, eye swelling, ocular discomfort, vision blurred, visual acuity reduced, eyelid disorder, erythema of eyelid, abnormal sensation in eye, eye dryness, blurred and/or diminished vision, epiphora, iritis, corneal ulcer, corneal infiltrates

Not known: Corneal damage, e.g. thinning, erosion, epithelial breakdown and perforation, endophthalmitis, ulcerative keratitis, corneal abrasion, intraocular pressure increased, photophobia, corneal disorder, blepharitis, eye discharge, corneal opacity, corneal infiltrates, corneal deposits, eye allergy, keratitis, corneal oedema, eyelid oedema, lacrimation increased, eye discharge, foreign body sensation in eyes

Respiratory, Thoracic, and Mediastinal Disorders

Uncommon: nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat)

Not known: Bronchospasm or exacerbation of asthma, dyspneoa

Gastrointestinal Disorders

Uncommon: vomiting

Not known: nausea

Hepatobiliary Disorders

Uncommon: alanine aminotransferase increased, gamma glutamyltransferase increased.

Cardiac Disorders

Not known: palpitations

Skin and Subcutaneous Tissue Disorders

Not known: erythema, rash, pruritus

Immune System Disorders

Not known: hypersensitivity including localized allergic reactions

None of the typical adverse reactions reported with the Anti-inflammatory agents (including ketorolac) have been observed at the doses used in topical ophthalmic therapy.

Paediatric population

Based on data from clinical trials involving paediatric patients, the type and severity of adverse reactions in the paediatric population are similar to those in adults

Overdosage

Data not available. Overdose is unlikely to occur via the recommended method of administration. If accidentally ingested, drink fluids to dilute.

Storage

Store between 15°C - 30 °C. Protect from light

Keep out of reach of children.

Shelf life

24 Months from the date of manufacture.

Presentation

A clear, greenish yellow colored solution filled in 5mL Sterile Gamma-irradiated white opaque LDPE bottle sealed with Sterile Gamma-irradiated natural transparent LDPE open nozzle and Sterile Gamma-irradiated white HDPE tamp safe cap in printed carton along with leaflet.

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.
Email: info@sensespharma.com

EKMP-02

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