Moxifloxacin with Dexamethasone Eye Drops 0.5%w/v & 0.1 %w/v

SENZMOX®-DX

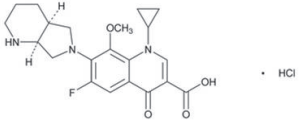
For the use of Registered Medical Practitioner only

Composition

Moxifloxacin Hydrochloride USP equivalent to
Moxifloxacin 0.5%w/v
Dexamethasone Sodium Phosphate USP equivalent to
Dexamethasone Phosphate 0.1%w/v
Benzalkonium Chloride Solution USP 0.01%v/v
(as preservative)
Water for Injection USP ..... q.s

Chemical Structure & Name

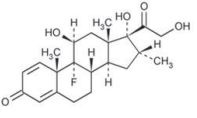
Moxifloxacin



(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* ,*7aS*)-octahydro-6*H* -pyrrolo[3,4-*b*]pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid, monohydrochloride

Dexamethasone



Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11•,16•)-. 9-Fluoro-11•,17,21-trihydroxy-16•-methylpregna-1,4-diene-3,20-dione.

Category

Pharmacotherapeutic group: Ophthalmologicals – Anti-inflammatory agents and antiinfectives in combination- corticosteroids and anti-infectives in combination- dexamethasone and anti-infectives

*ATC code:*S01CA01

Description:

A clear greenish yellow coloured solution filled in 10mL 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, a fourth-generation fluoroquinolone, inhibits the DNA gyrase and topoisomerase IV required for bacterial DNA replication, repair, and recombination.

Resistance:

Resistance to fluoroquinolones, including moxifloxacin generally occurs by chromosomal mutations in genes encoding DNA gyrase and topoisomerase IV. In Gram-negative bacteria, moxifloxacin resistance can be due to mutations in mar(multiple antibiotic resistances) and theqnr(quinolone resistance) gene systems. Resistance is also associated with expression of bacteria efflux proteins and inactivating enzymes. Cross-resistance with beta-lactams, macrolides and aminoglycosides is not expected due to differences in mode of action. 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

Staphylococcus aureus (methicillin susceptible)

Streptococcus pneumoniae

Streptococcus pyogenes

Streptococcus viridansGroup

Aerobic Gram-negative micro-organisms:

Enterobactercloacae

Haemophilusinfluenzae

Klebsiellaoxytoca

Moraxellacatarrhalis

Serratiamarcescens

Anaerobic micro-organisms:

Proprionibacterium acnes

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

Dexamethasone

Dexamethasone is a potent, long-term acting synthetic glucocorticoid class of steroid drugs that have anti-inflammatory and immunosuppressant properties.Dexamethasone has been demonstrated by animal and human studies based on oral application to possess approximately six to seven times the potency of prednisolone and at least 30 times the potency of cortisone. The potency of the compound is accomplished by the addition of a methyl radical and a fluorine atom to the prednisolone radical.

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 1,000 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.Moxifloxacin is widely distributed in the body and is excreted in feces or urine either unchanged or as glucuronide or sulfate conjugates.

Dexamethasone

Dexamethasone is absorbed rapidly after oral administration with a half-life of about 190 minutes. Sufficient absorption may occur after topical application to the skin and eye to produce systemic effects. In plasma Dexamethasone protein binding is less than for mostother corticosteroids. Corticosteroids diffuse into tissue fluids and cerebrospinal fluid but transplacental diffusion in significant amounts has not been demonstrated. Corticosteroids are metabolized in the liver the kidney and excrete in the urine. Metabolism is similar to other corticosteroids. Intraocular penetration occurs in significant amounts and contributes to the effectiveness of Dexamethasone in anterior segment inflammatory disease.

Indications

Moxifloxacin with Dexamethasone Eye Drops 0.5 % w/v & 0.1 % w/v 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.

Dosage & Administration

One or two drops instilled into the conjunctival sac(s), every 4 to 6 hours. During the initial 24 to 48 hours, the dosage may be increased to 1 or 2 drops every two hours. Frequency must be decreased gradually or warranted by improvement in clinical signs. Care should be taken not to discontinue the therapy prematurely.

Prevention of post-operative ocular inflammation & infection: Instill 1 drop qid in the eye, starting 1 day pre-operation & during 15 days post-operation.

Method of Administration:

As with any eye drops, to reduce possible systemic absorption, it is recommended that the lachrymal sac be compressed at the medial canthus (punctual occlusion) or eyelids are closed for two minutes. This should be performed immediately following the instillation of each drop. This may result in a decrease of systemic side effects and an increase in local activity.

To avoid contamination of the eye or eye drops do not allow the dropper tip to come into contact with any surface.

Contraindications

Moxifloxacin with Dexamethasone Eye Drops0.5 % w/v & 0.1 % w/vis 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.

Moxifloxacin with Dexamethasone Eye Drops0.5 % w/v & 0.1 % w/vis not recommended for use in children below 3 years.

Warning and Precaution

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 Moxifloxacin occurs, discontinue use of the medicinal product. Serious acute hypersensitivity reactions to moxifloxacin or any other product ingredient may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated.

Clinical manifestations may include one or more of the following: fever, rash or severe dermatologic reactions (e.g. toxic epidermal necrolysis, Stevens-Johnson Syndrome), vasculitis, arthralgia, myalgia, serum sickness, allergic pneumonitis, interstitial nephritis, acute renal insufficiency or failure, hepatitis, jaundice, acute hepatic necrosis or failure, anemia including hemolytic and aplastic, thrombocytopenia including thrombotic thrombocytopenicpurpura, leukopenia, agranulocytosis, pancytopenia, and/or other hematologic abnormalities.

As with other anti-infective, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If super infection occurs, discontinue use and institute alternative therapy.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy

includingmoxifloxacin, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration of Moxifloxacin plasma concentrations ofmoxifloxacin are much lower than after therapeutic oral doses of moxifloxacin, however, caution should be exercised and treatment with Moxifloxacin should be discontinued at the first sign of tendon inflammation.

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.

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

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 in such patients. Patients older than 2 years of age with eye infections caused by *Chlamydia trachomitis should* 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.*

Patients should be advised not to wear contact lenses if they have signs and symptoms of a bacterial ocular infection.

Prolonged use of topical ophthalmic corticosteroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, reduced visual acuity, visual field defects and posteriorsubcapsular cataract formation. During prolonged corticosteroid therapy, adrenal suppression and atrophy may occur and secretion of corticotrophin may be suppressed.

Abrupt withdrawal of corticosteroid therapy may precipitate acute adrenal insufficiency with muscle weakness, hypotension, hypoglycaemia, headache, nausea, vomiting, restlessness and muscle and joint pain. In patients receiving prolonged ophthalmic corticosteroid therapy, intraocular pressure and the lens should be checked routinely and frequently, particularly in patients with a history or presence of glaucoma. This is especially important in paediatric patients as the risk of corticosteroid-induced ocular hypertension may be greater in children and may occur earlier than in adults. The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes).

Topical corticosteroids should not be used for longer than one week except under ophthalmic supervision, with regular checks of intraocular pressure. Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral and fungal infections and mask the clinical signs of infections. In such cases, antibiotic therapy is mandatory. Fungal infection should be suspected in patients with persistent corneal ulceration and corticosteroids therapy should be discontinued if fungal infection occurs. Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chickenpox and measles, for example, can have a more serious or even fatal course in children on immunosuppressant corticosteroids. In such children, or in adults who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG), as appropriate, may be indicated. If chickenpox develops, treatment with antiviral agents may be considered. Children on long term steroids must be carefully observed for potential serious adverse reactions such as obesity, growth retardation, osteoporosis and adrenal suppression.

Topical ophthalmic corticosteroids may slow corneal wound healing. Topical NSAIDs are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.

Stress and intercurrent illness in patients on corticosteroid therapy subjected to unusual stress (from trauma or infection), increased dosage of rapidly acting corticosteroids before, during & after the stressful situation is indicated.

Drug induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual reduction of dosage. Muscle weakness and stiff joints may persist for 3-6 months after discontinuation of treatment. In some cases, withdrawal symptoms may simulate a clinical relapse of the disease for which the patient has been under treatment.

Use with caution in patients with impaired hepatic function, a reduction of dosage may be necessary. In treating chronic active liver disease with the

drug, major adverse reactions such as vertebral collapse, diabetes, hypertension, cataracts and Cushing's syndrome occur in about 30% of patients.

Caution is recommended for elderly patients as they are more susceptible to adverse reactions.

The possibility of development of osteoporosis should be an important consideration in initiating and managing corticosteroid therapy, especially in post-menopausal women.

Caution should be taken in patients with diabetes mellitus.

Patients should not be vaccinated with live vaccines while on corticosteroid therapy. Other immunization procedures should not be undertaken in patients on corticosteroid therapy, especially on high doses, because of possible hazards of neurological complications and lack of antibody response.

Immunization procedures may be undertaken in patients receiving corticosteroids as replacement therapy.

Contact lens wear is not recommended during treatment of an ocular inflammation. Additionally, this product contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. Patients must be instructed to remove contact lenses prior to application of Moxifloxacin with Dexamethasone Eye Drops and wait at least 15 minutes before reinsertion.

There is no evidence of safety in use in children under two years of age.

Moxifloxacin may cause temporary blurred vision or other visual disturbances, which may affect the ability to drive or use machines. Dexamethasone has no or negligible influence on the ability to drive and use machines, however, 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 specific interaction studies have been performed with Moxifloxacin solution. Given the low systemic concentration of moxifloxacin following topical ocular administration of the medicinal product, drug interactions are unlikely to occur.

Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems

Drugs which induce hepatic microsomal enzymes, such as barbiturates, phenytoin and rifampicin, administered before or during treatment may shorten the elimination half-life of Dexamethasone. Long term corticosteroid therapy may also reduce the half-life. Oral contraceptives have been reported to increase the volume of distribution.

The risk of increased intraocular pressure associated with prolonged corticosteroid therapy may be more likely to occur with concomitant use of anticholinergics, especially atropine and related compounds, in patients predisposed to acute angle closure.

The risk of corneal deposits or corneal opacity may be more likely to occur in patients presenting with compromised cornea and receiving polypharmacy with other phosphatecontaining eye medications.

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

Pregnancy & Lactation

There are no adequate data from the use of Moxifloxacin as well as Dexamethasone in pregnant women. However, no effects on pregnancy are anticipated since the systemic exposure to Moxifloxacin and

Dexamethasone Eye Drops is negligible. The medicinal product is not recommended during pregnancy unless the clinical condition of the woman requires treatment with moxifloxacin and dexamethasone.

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 Moxifloxacin no effects on the suckling child are anticipated. Whereas systemically administered corticosteroids

System Organ Classification	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Rare	haemoglobin decreased
	Not Known	hypersensitiviy
Immune system disorders	Uncommon	Headache
	Rare	paresthesia
	Not Known	diziness
Nervous system disorders	Common	eye pain, eye irritation
	Not known	punctate keratitis, dry eye, conjunctivalhaemorrhage, ocular hyperaemia, eye pruritus, eyelid oedema, ocular discomfort
Eye disorders	Rare	corneal epithelium defect, corneal disorder, conjunctivitis, blepharitis, eye swelling, conjunctivaloedema, vision blurred, visual acuity reduced,asthenopia, erythema of eyelid
	Not known	endophthalmitis, ulcerative keratitis,corneal erosion, corneal abrasion,intraocular pressure increased, cornealopacity, corneal infiltrates, cornealdeposits, eye allergy, keratitis, cornealoedema, photophobia, , eyelid oedema, lacrimation increased, eyedischarge, foreign body sensation in eyes.
Cardiac disorders	Not known	Palpitations
Respiratory, thoracic and mediastinal disorders	Rare	nasal discomfort, pharyngolaryngeal pain, sensation of foreign body(throat)
	Not known	dyspnoea
Gastro-intestional disorders	Uncommon	Dysgeusia
	Rare	Vomiting
	Not known	Nausea
Hepatobiliary disorders	Rare	alanine aminotransferase increased, gamma-glutamyltransferase increased
Skin and subcutaneous tissue disorders	Not known	erythema, rash, pruritus, urticarial

appear in human milk in quantities that could affect the child being breastfed. However, when instilled topically, systemic exposure is low. It is unknown whether Dexamethasone is excreted in human milk.

A risk to the suckling child cannot be excluded. The medicinal product is not recommended to be used during breast-feeding.

Adverse reaction

The following adverse reactions 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) or not known (cannot be estimated).

Overdosage

The limited holding capacity of the conjunctival sac for ophthalmic products practically precludes any overdosing of the medicinal product.

The total amount of moxifloxacin in a single container is too small to induce adverse effects after accidental ingestion. Long-term intensive topical use may lead to systemic effects. Oral ingestion of the contents of the bottle (up to 10 mL) is unlikely to lead to any serious adverse effects.

An ocular overdose of Moxifloxacin & Dexamethasone can be flushed from the eye(s) with lukewarm water.

Storage

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

Keep out of reach of children.

Shelf life

24 Months from the date of manufacturing.

Presentation

A clear greenish yellow coloured solution filled in 10mL 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.,

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Email: info@sensespharma.com

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