Centaflox®-Dx
Eye Drops

1. Generic Name

Moxifloxacin Hydrochloride and Dexamethasone Sodium Phosphate Eye Drops.

2. Qualitative and Quantitative Composition

Moxifloxacin Hydrochloride IP

Equivalent to Moxifloxacin ……..…..0.5% w/v

Dexamethasone Sodium Phosphate IP

Equivalent to Dexamethasone Phosphate …….0.1% w/v

Sterile aqueous buffered vehicle ……..q.s

3. Dosage form and strength

Topical ophthalmic solution containing Moxifloxacin Hydrochloride 0.5% w/v and Dexamethasone 0.1% w/v.

4. Clinical particulars

4.1 Therapeutic indication

- Ocular infections caused by susceptible organisms.

- Inflammation and infections after ocular surgery

4.2 Posology and method of administration

Instil one drop in the affected eye 3 times a day for 5 to 7 days or as directed by the physician.

4.3 Contraindication

Moxifloxacin 0.5% ophthalmic solution is contraindicated in patients with a history of hypersensitivity to Moxifloxacin, to other quinolones, or to any of the components in this medication.

The use of Centaflox-Dx eye drops is also contraindicated in epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, and in other viral diseases of the conjunctiva and cornea, mycobacterial infection of the eye and fungal diseases of ocular structures

4.4 Special warnings and precautions for use

Moxifloxacin 0.5% 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, dyspnoea, urticaria and itching).

If an allergic reaction to Moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment.

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

Caution is also necessary when used in conjunction with antiviral therapy in the treatment off stromal keratitis or uveitis.

Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral and fungal infections and mask the clinical signs of infections, preventing recognition of ineffectiveness of the antibiotic. In such cases antibiotic therapy is mandatory. Fungal infection should be suspected in patients with persistent corneal ulceration who have been or are receiving these drugs, and corticosteroid therapy should be discontinued if fungal infection occurs.

Topical corticosteroids should not be used longer than one week except under ophthalmic supervision. Prolonged use of topical ophthalmic corticosteroids may result in increased intraocular pressure, ocular hypertension, with damage the optic nerve, reduced visual acuity, visual field defects and posterior subcapsular cataract formation. In patients receiving prolonged ophthalmic corticosteroid therapy, intraocular pressure and lens should checked routinely and frequently, particularly in patients with a history or presence of glaucoma. The dose anti-glaucoma medication may need to be adjusted in these patients. Prolonged use may increase the hazard of secondary ocular infections. Topical ophthalmic corticosteroids may slow corneal wound healing.

Cushing's syndrome and/or adrenal suppression associated with systemic absorption of ocular dexamethasone may occur after intensive or long-term continuous therapy in predisposed patients, including children and patients treated with CYP3A4 inhibitors (including ritonavir and cobicistat). In these cases, treatment should be progressively discontinued.

Contact lenses should not be worn during the treatment with corticosteroid eye drops due to increased risk of infection.

4.5 Drug interactions

Moxifloxacin

Drug-drug interaction studies have not been conducted with Moxifloxacin 0.5% ophthalmic solution.

Dexamethasone

The risk of increased intraocular pressure associated with prolonged corticosteroid therapy may be more likely to occur with concomitant use of anti-cholinergic, 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 phosphate containing eye medications. The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Dexamethasone: The therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin. Glucocorticoids may increase the need for salicylates as plasma salicylate clearance is increased. 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.

4.6 Use in special population

Paediatric: The safety and effectiveness of Moxifloxacin in infants below 1 year of age have not been established.

Geriatric: No overall differences in safety and effectiveness have been observed between elderly and other adult patients.

Liver impairment: No data found.

Renal failure: No data found.

Pregnancy and lactation: Since there are no adequate and well-controlled studies in pregnant women, Centaflox-Dx eye drops should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Centaflox-Dx eye drops is known.

4.8 Undesirable effects

In clinical trials the most frequently reported ocular adverse events were: decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperaemia, ocular pain, ocular pruritus, subconjunctival haemorrhage, and tearing. These events occurred in approximately 1-6% of patients.

4.9 Overdose

There is limited experience of overdose with Centaflox-Dx eye drops. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

Moxifloxacin is a synthetic fluoroquinolone antibacterial agent active in vitro against a broad spectrum of Gram-positive and Gram-negative ocular pathogens, atypical microorganisms and anaerobes. The antibacterial action of Moxifloxacin results from inhibition of 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.

Dexamethasone is a highly potent and long-acting glucocorticoid. The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroids will inhibit phospholipase A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins. Corticosteroids also produce a marked, though transient, lymphocytopenia. This depletion is due to redistribution of the cells; the T lymphocytes being affected to a greater degree than the B lymphocytes. Lymphokine production is reduced, as is the sensitivity of macrophages to activation by lymphokines. Corticosteroids also retard epithelial regeneration, diminish post-inflammatory neo-vascularisation and reduce towards normal levels the excessive permeability of inflamed capillaries. The actions of corticosteroids described above are exhibited by dexamethasone and they all contribute to its anti-inflammatory effect.

5.2 Pharmacodynamic properties

Moxifloxacin is a fluoroquinolone antibiotic. Moxifloxacin can be used to treat infections caused by the following bacteria: Aerobic Gram-positive microorganisms: Corynebacterium species, Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus warneri, Streptococcus pneumoniae, and Streptococcus viridans group. Aerobic Gram-negative microorganisms: Acinetobacter lwoffii, Haemophilus influenzae, and Haemophilus parainfluenzae. Other microorganisms: Chlamydia trachomatis.

Moxifloxacin is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian. Moxifloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria.

Dexamethasone and its derivatives, dexamethasone sodium phosphate and dexamethasone acetate, are synthetic glucocorticoids. Used for its anti-inflammatory or immunosuppressive properties and ability to penetrate the CNS, dexamethasone is used alone to manage cerebral oedema and with tobramycin to treat corticosteroid-responsive inflammatory ocular conditions.

5.3 Pharmacokinetic properties

Moxifloxacin

Moxifloxacin is readily absorbed from the gastrointestinal tract after oral doses with an absolute bioavailability of about 90%. It is widely distributed throughout the body tissues and is about 30 to 50% bound to plasma proteins. Moxifloxacin has an elimination half-life of about 12 hours, allowing once-daily dosing. It is metabolised mainly via sulfate and glucuronide conjugation, and is excreted in the urine and the faeces as unchanged drug and as metabolites, the sulfate conjugate primarily in the faeces and the glucuronide exclusively in the urine. Distribution into milk has been found in animals.

Dexamethasone

Absorption

When given topically to the eye, Dexamethasone is absorbed into the aqueous humour, cornea, iris, choroid, ciliary body and retina. Systemic absorption occurs but may be significant only at higher dosages or in extended paediatric therapy. Up to 90% of dexamethasone is absorbed when given by mouth; peak plasma levels are reached between 1 and 2 hours after ingestion and show wide individual variations.

Distribution

Tissue distribution studies in animals show a high uptake of dexamethasone by the liver, kidney and adrenal glands; a volume of distribution has been quoted as 0.58 l/kg. In man, over 60% of circulating steroids are excreted in the urine within 24 hours, largely as unconjugated steroid.

Metabolism

Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Up to 77% of dexamethasone is bound to plasma proteins, mainly albumin. This percentage, unlike cortisol, remains practically unchanged with increasing steroid concentrations. The mean plasma half-life of dexamethasone is 3.6 ± 0.9h.

Distribution

Dexamethasone also appears to be cleared more rapidly from the circulation of the foetus and neonate than in the mother; plasma dexamethasone levels in the foetus and the mother have been found in the ratio of 0.32:1.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Moxifloxacin

In vitro studies of fluoroquinolones with human or rabbit corneal epithelial cells or keratocytes suggest that moxifloxacin is similar in cytotoxicity potential to other drugs of this family. Specialized in vivo corneal wound-healing studies draw little distinction between moxifloxacin-treated eyes and those treated with other fluoroquinolones. Repeated-dose topical ocular studies in rabbits and monkeys, with high concentrations (up to 3%) of moxifloxacin and at treatment durations and regimens well in excess of label-prescribed use, demonstrated a high safety margin for ocular and extraocular tissues. Cornea, the tissue with highest exposure, was found to be unaffected by these high exposures, with slitlamp biomicroscopy, corneal thickness measurement, intraocular pressure, and specular microscopy of the corneal endothelium (monkeys only), and histologic evaluation showing no effects, as compared with controls. Moxifloxacin ophthalmic solution 0.5% affords superior efficacy and ocular tissue penetration, with a favourable safety profile.

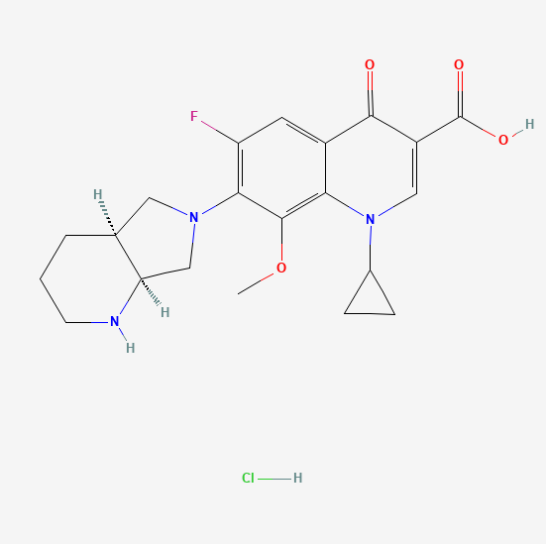
Dexamethasone

Female rabbits (n=6/group) received dexamethasone phosphate (40 mg/mL ophthalmic solution, EGP-437) transscleral to the right eye (OD) using the Eyegate(®) II ocular iontophoresis delivery system once biweekly for 24 consecutive weeks at current doses of 10, 14, and 20 mA-min and current levels up to, and including -4 mA for 3.5-5 min.

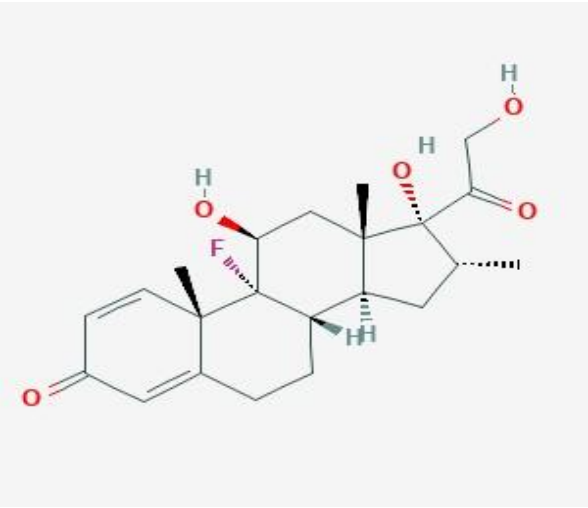
The biweekly transscleral iontophoresis with either the citrate buffer or dexamethasone phosphate at cathodic doses up to and including 20 mA-min and currents up to, and including -4 mA for 24 weeks was well-tolerated. Transient signs of conjunctival hyperemia and chemosis, mild corneal opacity, and fluorescein staining of the cornea were noted and attributed to expected ocular reactions to the temporary placement of the ocular applicator and application of iontophoresis. There was no dexamethasone phosphate-, dexamethasone-, or iontophoresis-related effects on IOP, electroretinography, or histopathology. Reductions in body weight gain, anaemia, decreased leukocyte and lymphocyte counts, compromised liver function, enlarged liver, and reduced spleen weight were consistent with systemic corticosteroid-mediated pharmacology, repeated use of anaesthesia, stress, and sedentariness, and unlikely to be related to iontophoresis application.

7. Description

Moxifloxacin Hydrochloride is the hydrochloride salt of a fluoroquinolone antibacterial antibiotic. Its chemical name is 7-[(4aS,7aS)-1,2,3,4,4a,5,7,7a-octahydropyrrolo[3,4-b]pyridin-6-yl]-1-cyclopropyl-6-fluoro-8methoxy-4-oxoquinoline-3-carboxylic acid, hydrochloride. The empirical formula and molecular weight is $C_{21}H_{25}ClFN_3O_4$ and 437.9g/mol.



Dexamethasone is a synthetic adrenal corticosteroid with potent anti-inflammatory properties. Its chemical name is (8S,9R,10S,11S,13S,14S,16R,17R)-9-fluoro-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13,16-trimethyl-6,7,8,11,12,14,15,16-octahydrocyclopenta[a]phenanthren-3-one. The empirical formula and molecular weight is $C_{22}H_{29}FO_5$ and 392.5 g/mol.



8. **Pharmaceutical particulars**

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

Centaflox-Dx eye drops is available in 5ml.

8.4 Storage and handling instructions

Store below $30^{O}C$, protected from light. Do not freeze.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by

CENTAUR PHARMACEUTICALS PVT. LTD.
Plant I, Plot No. 3, 5B, 2C, Tivim
Industrial Estate, Karaswada,
Mapusa, Goa - 403 526.

11. Details of permission or license number with date :

Mfg Lic.No. 176, Dated – 09.10.2015

12. Date of revision: December 2025