Centaflox®-Dx

1. Composition

Moxifloxacin	0.5% w/v
Dexamethasone	0.1%

2. Dosage form and strength

Centaflox-Dx eye drops is available in 5ml in plastic bottle.

3. Clinical particulars

3.1 Therapeutic indication

- In post-surgery infection
- Inflammation

3.2 Posology and method of administration

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

3.3 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.

3.4 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.
- If an allergic reaction to Moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment.
- 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.
- Adrenocortical Insufficiency Drug induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual reduction of dosage.
- Infection Corticosteroids may mask some signs of infection (such as fever and inflammation), and new infections may appear during their use.

- There may be decreased resistance and inability to localise infection when corticosteroids are used.
- Ophthalmological Complications Prolonged use of corticosteroids may produce posterior subcapsular cataracts or glaucoma with possible damage to optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.
- 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.

3.5 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.

3.6 Use in special population

- Paediatric: The safety and effectiveness of Moxifloxacin 0.5% ophthalmic solution 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, Moxifloxacin 0.5% ophthalmic solution should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

3.7 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.

3.8 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.

3.9 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.

4. Pharmacological properties

4.1 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, lymphocytopaenia. 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.

4.2 Pharmacodynamic properties

Moxifloxacin is a quinolone/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 edema and with tobramycin to treat corticosteroid-responsive inflammatory ocular conditions.

4.3 Pharmacokinetic properties

- 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

<u>Absorption</u>

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.

5. Nonclinical properties

5.1 Animal Toxicology or Pharmacology

Not required.

6. Description

Already mentioned and covered in the above points.

7. Pharmaceutical particulars

7.1 Incompatibilities

There are no known incompatibilities.

7.2 Shelf-life

24 months.

7.3 Storage and handling instructions

Store in cool and dry place.