1.5.1 Prescribing information (Summary of Product Characteristics):

1. NAME OF THE MEDICINAL PRODUCT

1.1.Product Name

MOSI-D Eye Drops (Moxifloxacin and Dexamethasone Eye Drops)

1.2.Strength

Each ml contains Dexamethasone BP ….1 mg Moxifloxacin …. 5 mg
(As Moxifloxacin Hydrochloride USP) Aqueous buffered vehicle. ….qs Benzalkonium Chloride USP/NF ……0.05 mg (As preservative)

1.3.Pharmaceutical form

Eye Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION Composition:

Each ml contains Dexamethasone BP ……. 1 mg Moxifloxacin ……..... 5 mg
(As Moxifloxacin Hydrochloride USP) Aqueous buffered vehicle. ….qs Benzalkonium Chloride USP/NF ……0.05 mg (As preservative)

3. Pharmaceutical form

Eye drops (solution).
A clear, yellow colored solution.

4. Clinical particulars

4.1.Therapeutic indications

MOSI D is indicated for the short-term treatment of steroid responsive conditions of the eye when prophylactic antibiotic treatment is also required, after excluding the presence of fungal and viral disease. It may include the following conditions:

- In patients with blepharitis
- For topical prophylaxis and reduction of inflammation in phacoemulsification

4.2.Posology and method of administration

For ocular use only. Not for injection.
MOSI D eye drop should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye.

- In patients with blepharitis: Instill one drop of medication four times per day for 7 days.
- For topical prophylaxis and reduction of inflammation in phacoemulsification: Instill one drop of medication four times daily before and until 15 days after surgery.

The preparation is meant for adult patients only. No data is available for use in pediatric population.
To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle.
If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart.
Eye ointments should be administered last.

4.3.Contraindications

Use is contra-indicated in herpes simplex and other viral diseases of the cornea and conjunctiva, fungal disease, ocular tuberculosis, untreated purulent infections, patients with a history of acute epithelial herpes simplex keratitis or hypersensitivity to any component of the preparation.

4.4.Special warnings and precautions for use

For topical ophthalmic use only. Not for injection into the eye.

Dexamethasone

In those diseases causing 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 of stromal keratitis or uveitis and use of periodic slit-lamp microscopy.

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 corticosteroids therapy should be discontinued if fungal infection occurs.

Topical corticosteroids should not be used for longer than one week except under ophthalmic supervision. 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 posterior subcapsular cataract formation. 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. The dose of anti-glaucoma medication may need to be adjusted in these patients. Prolonged use may also increase the hazard of secondary ocular infections. Topical ophthalmic corticosteroids may slow corneal wound healing.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops.

Moxifloxacin

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.

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.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including moxifloxacin, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration of moxifloxacin, the plasma concentrations 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.

Moxifloxacin should not be used for the prophylaxis or empiric treatment of gonococcal conjunctivitis, including gonococcal ophthalmia neonatorum, 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.
MOSI D eye drop contains the preservative benzalkonium chloride, which may cause eye irritation. Contact lenses should be removed prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

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

Dexamethasone

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 following drug interactions are possible, but are unlikely to be of clinical significance, following the use of dexamethasone 0.1% w/v eye drops in the eye:

- 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.
- CYP3A4 inhibitors (including ritanovir and cobicistat) may decrease dexamethasone clearance resulting in increased effects and adrenal suppression/Cushing's syndrome. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid effects.

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.

Moxifloxacin

No specific interaction studies have been performed with moxifloxacin 0.5%w/v eye drops, solution. 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

Pregnancy

There are no or limited amount of data from the use of dexamethasone and moxifloxacin eye drops in pregnant women. Studies in animals have shown that topically applied steroids can be absorbed systemically and can cause abnormalities of foetal development in pregnant animals; although the relevance of these findings to human beings has not been established.

While, no effects on pregnancy are anticipated since the systemic exposure to moxifloxacin is negligible.

Breast-feeding mothers
Systemically administered corticosteroids appear in human milk in quantities that could affect the child being breastfed. Animal studies have shown excretion of low levels in breast milk after oral administration of moxifloxacin. However, when instilled topically, systemic exposure is low. It is unknown whether dexamethasone plus moxifloxacin/metabolites are excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from dexamethasone plus moxifloxacin therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7.Effects on ability to drive and use machines
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. Warn patients not to drive or operate hazardous machinery until vision is clear.

4.8.Undesirable effects
The common side effects which may occur with moxifloxacin-dexamthasone eye drops are: intraocular pressure increased (after 2 weeks of treatment), ocular discomfort after instillation, irritation, pain, burning, eye pruritus and blurred vision.

5. Pharmacological properties
5.1.Pharmacodynamic properties
Dexamethasone
Dexamethasone is a highly potent and long-acting glucocorticoid. It has an approximately 7 times greater anti-inflammatory potency than prednisolone. The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroid receptors are present in human trabecular meshwork cells and in rabbit iris ciliary body tissue. Corticosteroids will inhibit phospholipase A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins.
Moxifloxacin
Moxifloxacin, a fourth-generation fluoroquinolone, inhibits the DNA gyrase and topoisomerase IV required for bacterial DNA replication, repair, and recombination. Commonly susceptible species to moxifloxacin is shown in the table below:

COMMONLY SUSCEPTIBLE SPECIES
Aerobic Gram-positive micro-organisms:
Corynebacterium species including

Corynebacterium diphtheriae
Staphylococcus aureus (methicillin susceptible)
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus viridans
Group
Aerobic Gram-negative micro-organisms*:*
Enterobacter cloacae
Haemophilus
influenzae Klebsiella
oxytoca Moraxella
catarrhalis Serratia
marcescens
Anaerobic micro-

5.2.Pharmacokinetic properties

Dexamethasone

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.

Moxifloxacin

Following topical ocular administration of moxifloxacin, it 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 Cmax and 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 mean Cmax and AUC reported after therapeutic 400 mg oral doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

5.3.Preclinical safety data

Dexamethasone

Repeat dose topical ocular safety studies with dexamethasone in rabbits have shown systemic corticosteroid effects. Such effects are considered to be unlikely when dexamethasone eye drops are used as recommended.
Dexamethasone was clastogenic in the in vitro human lymphocyte assay and in vivo in the mouse micronucleus assay at doses in excess of those obtained following topical application. Conventional carcinogenicity studies with dexamethasone have not been performed.

Dexamethasone has been found to be teratogenic in animal models. Dexamethasone induced abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development.

Moxifloxacin

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure following administration to the eye indicating little relevance to clinical use.

As with other quinolones, moxifloxacin was also genotoxic in vitro in bacteria and mammalian cells. As these effects can be traced to the interaction with bacterial gyrase and in considerably higher concentrations to the interaction with topoisomerase II in mammalian cells, a threshold level for genotoxicity can be assumed. In in vivo tests, no evidence of genotoxicity was found, despite high doses of moxifloxacin. The therapeutic doses for human use therefore provide adequate safety margin. No indication of a carcinogenic effect was observed in an initiation promotion model in rats.

Unlike other quinolones, moxifloxacin showed no phototoxic or photogenotoxic properties in extensive in vitro and in vivo studies.

6. Pharmaceutical particulars

6.1.List of excipients:

Hydroxypropyl Betadex USP, Disodium Edetate BP, Sodium Chloride BP, Boric Acid BP, Benzalkonium Chloride NF, Sodium Hydroxide BP, Water for injection BP.

6.2.Incompatibilities – Not applicable

6.3.Shelf life – 18 months

Shelf Life after opening: Use the solution within one month after opening the vial.

6.4.Special precautions for storage – Store at a temperature not exceeding 30°C. Protect from light.

6.5.Nature and contents of container – 5 ml LDPE vial with HIPS cap

6.6.Special precautions for disposal and other handling - Not applicable

7. Marketing authorisation holder:

FDC Limited,
142 - 48 SV Road, Jogeshwari (West)
Mumbai 400 102 **India.**

8. Marketing authorisation number(s) – TAN 21 HM 0371

9. Date of first authorisation/renewal of the authorization – 2021-10-09

10. Date of revision of the text – Not applicable