Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

CIPROGLAX-D (Ciprofloxacin & Dexamethasone Eye Drops)

2. Qualitative and quantitative composition

Each ml contains:
Ciprofloxacin hydrochloride 3.85mg
Dexamethasone.....1.1mg

Excipients with known effect:
Benzalkonium chloride solution

For full list of excipients see section 6.1

3. Pharmaceutical form

Eye drops

4. Clinical particulars

4.1 Therapeutic indications

CIPROGLAX-D Eye Drops are indicated for the treatment of post-operative inflammatory conditions of the eyes.

4.2 Posology and method of administration

For Ophthalmic use

One or two drops of CIPROGLAX-D Eye Drops to be instilled into the conjunctival sac every 4–6 hours.

4.3 Contraindications

A history of hypersensitivity to ciprofloxacin, dexamethasone or any other component of the medication is a contraindication to its use.
A history of hypersensitivity to other quinolones may also contraindicate the use of ciprofloxacin.
Use is contraindicated 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

General

NOT FOR INJECTION INTO THE EYE. FOR TOPICAL USE ONLY.
The clinical experience in children less than 1 year old, particularly in neonates, is very limited. The use of CIPROGLAX-D Eye Drops in neonates with ophthalmia neonatorum of gonococcal or chlamydial origin is not

recommended as it has not been evaluated in such patients. Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition.

When using CIPROGLAX-D Eye Drops one should take into account the risk of rhino pharyngeal passage, which can contribute to the occurrence and the diffusion of bacterial resistance.

Serious, and occasionally fatal, hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnea, urticaria and itching. Only a few patients had a history of hypersensitivity reactions.
Serious acute anaphylactic reactions require immediate emergency treatment with epinephrine and other resuscitation measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines and airway management, as clinically indicated.

CIPROGLAX-D Eye Drops should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

As with all antibacterial preparations, prolonged use may lead to overgrowth of non-susceptible bacterial strains or fungi. If superinfection occurs, appropriate therapy should be initiated.

Remove contact lenses before using. During therapy, soft contact lenses should not be worn.

Ciprofloxacin
As with other antibacterial preparations, prolonged use of ciprofloxacin may result in overgrowth of non-susceptible organisms, including fungi. If super-infection occurs, appropriate therapy should be initiated. Whenever clinical judgement dictates, the patient should be examined with the aid of magnification, such as slit-lamp bio microscopy and, where appropriate, fluorescein staining.

Ciprofloxacin should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity reaction.

In clinical studies of patients with bacterial corneal ulcers, a white crystalline precipitate located in the superficial portion of the corneal defect was observed in 35 (16.6%) of 210 patients. The onset of the precipitate was within 24 hours to 7 days after starting therapy. In 1 patient, the precipitate was immediately irrigated out upon its appearance. In 17 patients, resolution of the precipitate was seen in 1–8 days (in 7 days if treated within the first 24–72 hours). In 5 patients, resolution was noted in 10–13 days. In 9 patients, exact resolution days were unavailable; however, at follow-up examinations, 18–44 days after onset of the event, complete resolution of the precipitate was noted. In 3

patients, outcome information was unavailable. The precipitate did not preclude continued use of ciprofloxacin, nor did it adversely affect the clinical course of the ulcer or visual outcome.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy, including ciprofloxacin, particularly in elderly patients and those treated concurrently with corticosteroids. Therefore, treatment with ciprofloxacin eye drops should be discontinued at the first sign of tendon inflammation.

During therapy, soft contact lenses should not be worn. Contact lens wear is not recommended during treatment of an ocular infection. Therefore, patients should be advised not to wear contact lenses during treatment with CIPROGLAX-D Eye Drops.

Dexamethasone
General
The possibility of persistent fungal infections of the cornea should be considered after prolonged corticosteroid dosing. There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Warnings
Prolonged use may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision, and posterior subcapsular cataract formation. Prolonged use may suppress the host response and, thus, increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids. In acute purulent conditions of the eye or ear, corticosteroids may mask infection or enhance existing infection. If these products are used for 10 days or longer, intraocular pressure should be routinely monitored even though it may be difficult in children and uncooperative patients.

Employment of corticosteroid medication in the treatment of herpes simplex other than epithelial herpes simplex keratitis, in which it is contraindicated, requires great caution; periodic slit-lamp microscopy is essential.

Hypersensitivity Reactions
CIPROGLAX-D Eye Drops should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolones. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal, or facial edema), airway obstruction, dyspnea, urticaria, and itching.

Continued or Recurrent Otorrhea
If otorrhea persists after a full course of therapy, or if two or more episodes of otorrhea occur within six months, further evaluation is recommended to exclude an underlying condition such as cholesteatoma, foreign body, or a tumor.

4.5 Interaction with other medicinal products and other forms of interaction
Specific drug interaction studies have not been conducted with ciprofloxacin and dexamethasone eye drops. However, the systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, enhance the effects of the oral anticoagulant, warfarin and its derivatives, and has been associated with transient elevations in serum creatinine in patients receiving cyclosporine concomitantly.

4.6 Pregnancy and Lactation
Pregnancy
Category C
Reproduction studies have been performed in rats and mice at doses up to 6 times the usual daily human oral dose and have revealed no evidence of impaired fertility or harm to the fetus due to ciprofloxacin. In rabbits, as with most antimicrobial agents, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion. No teratogenicity was observed at either dose. After intravenous administration, at doses up to 20 mg/kg, no maternal toxicity was produced and no embryotoxicity or teratogenicity was observed.
There are no adequate and well-controlled studies in pregnant women. **CIPROGLAX-D Eye Drops** should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Dexamethasone has been shown to be teratogenic in mice and rabbits following topical ophthalmic application in multiples of the therapeutic dose. In the mouse, corticosteroids produce fetal resorptions and a specific abnormality, cleft palate. In the rabbit, corticosteroids have produced fetal resorptions and multiple abnormalities involving the head, ears, limbs, palate, etc.
There are no adequate or well-controlled studies in pregnant women. Dexamethasone sodium phosphate eye drops should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

Lactating Women
It is not known whether topically applied ciprofloxacin is excreted in human milk; however, it is known that orally administered ciprofloxacin is excreted

in the milk of lactating rats and oral ciprofloxacin has been reported in human breast milk after a single 500 mg dose.
Topically applied steroids are absorbed systemically. Therefore, because of the potential for serious adverse reactions in nursing infants from dexamethasone, caution should be exercised when CIPROGLAX-D Eye Drops are administered to a nursing mother. A decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Fertility

Studies have not been performed in humans to evaluate the effect of topical administration of ciprofloxacin on fertility. Oral administration in animals does not indicate direct harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

This product has no or negligible influence on the ability to drive or use machines.

Temporarily blurred vision or other visual disturbances may affect the ability to drive or use machines. If transient blurred vision occurs upon instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

Ciprofloxacin

Because clinical studies are conducted under widely varying conditions, adverse drug reaction rates observed in the clinical studies of a drug cannot be directly compared with rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

The most frequently reported drug-related adverse reaction was local burning and discomfort. In corneal ulcer studies with frequent administration of the drug, white crystalline precipitates were seen in approximately 17% of patients. Other reactions occurring in less than 10% of patients included lid margin crusting, crystals/scales, foreign body sensation, itching, conjunctival hyperemia, and a bad taste following instillation. Additional events occurring in less than 1% of patients included corneal staining, keratopathy/keratitis, allergic reactions, lid oedema, tearing, photophobia, corneal infiltrates, nausea and decreased vision. Hypersensitivity reactions cannot be excluded.

The adverse reactions listed below 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 from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions have been observed during clinical trials and postmarketing experience.

The following undesirable effects were reported in association with the use of ciprofloxacin eye drops:

System Organ Classification	**MedDRA Preferred Term (v. 15.1)**
Infections and infestations	***Rare:*** hordeolum, rhinitis
Immune system disorders	***Rare:*** hypersensitivity
Nervous system disorders	***Common:*** dysgeusia ***Uncommon:*** headache ***Rare:*** dizziness
Eye disorders	***Common:*** corneal deposits, ocular discomfort, ocular hyperemia ***Uncommon:*** keratopathy, corneal infiltrates, corneal staining, photophobia, visual acuity reduced, eyelid oedema, blurred vision, eye pain, dry eye, eye swelling, eye pruritus, foreign body sensation in eyes, lacrimation increased, eye discharge, eyelid margin crusting, eyelid exfoliation, conjunctival oedema, erythema of eyelid ***Rare:*** ocular toxicity, punctate keratitis, keratitis, conjunctivitis, corneal disorder, corneal epithelium defect, diplopia, hypoesthesia eye, asthenopia, eye irritation, eye inflammation, conjunctival hyperemia
Ear and labyrinth disorders	***Rare:*** ear pain
Respiratory, thoracic and mediastinal disorders	***Rare:*** paranasal sinus hypersecretion, rhinitis
Gastrointestinal disorders	***Uncommon:*** nausea ***Rare:*** diarrhea, abdominal pain
Skin and subcutaneous tissue disorders	***Rare:*** dermatitis
General disorders and administration site	***Rare:*** drug intolerance

conditions	
Musculoskeletal and connective tissue disorders	***Not known:*** *tendon disorder*
Investigations	***Rare:*** laboratory test abnormal

Description of Selected Adverse Events

With locally applied fluoroquinolones, (generalized) rash, toxic epidermolysis, dermatitis exfoliative, Stevens-Johnson syndrome and urticaria occur very rarely.

Serious, and occasionally fatal, hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnea, urticaria, and itching.

In patients with corneal ulcers and frequent administration of the drug, white precipitates have been seen with locally applied fluoroquinolones; (generalized) rash, toxic epidermolysis, dermatitis exfoliative, Stevens-Johnson syndrome and urticaria occur very rarely.

Ruptures of the shoulder, hand, Achilles' tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and postmarketing experience with systemic fluoroquinolones indicate that the risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress, including the Achilles' tendon. To date, clinical and postmarketing data have not demonstrated a clear association between ciprofloxacin eye drops and musculoskeletal and connective tissue adverse reactions.

In isolated cases, blurred vision, decreased visual acuity and medication residue have been observed with ophthalmic ciprofloxacin.

Safety and effectiveness of ciprofloxacin eye drops were determined in 230 children between the ages of 0 and 12 years. No serious adverse drug reaction was reported in this group of patients.

Systemic Absorption of fluoroquinolones has been reported to cause following adverse effects:

The drug may cause low blood sugar and mental health related side effects. Low blood sugar levels, also called hypoglycemia, can lead to coma. The mental health side effects more prominent and more consistent across the systemic fluoroquinolone drug class are as mentioned below;

- Disturbances in attention
- Disorientation
- Agitation
- Nervousness
- Memory impairment
- Serious disturbances in mental abilities called delirium

Dexamethasone

Glaucoma with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, perforation of the globe has been reported.

Rarely, filtering blebs have been reported when topical steroids have been used following cataract surgery.

Rarely, stinging or burning may occur.

The following undesirable effects 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 from the available data).

Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Endocrine Disorders

NOT KNOWN (cannot be estimated from the available data): Cushing's syndrome, adrenal suppression

Ocular disorders

VERY COMMON (>1/10): intraocular pressure increased (after 2 weeks of treatment).

COMMON (>1/100, <1/10): ocular discomfort after instillation, irritation, burning, eye pruritus and blurred vision. These symptoms are mild and transient with no consequences.

UNCOMMON (>1/1,000, <1/100): signs and symptoms of allergic or hypersensitive reactions can occur. The following corticoid specific undesirable effects can occur: delay in healing, risk of posterior subcapsular cataract formation, opportunist infections and glaucoma.

VERY RARE (<1/10,000, including isolated reports): conjunctivitis, eyelid oedema, corticoid-induced uveitis, keratitis, corneal thinning, corneal oedema and ulcerations. Cases of corneal calcification have been reported in association with the use of phosphate-containing eye drops in some patients with significantly damaged corneas. Due to the steroid component, in diseases causing thinning of the cornea or sclera, there is a higher risk for perforation, especially after topical long treatments.

General Disorders and Administration Site Conditions

UNCOMMON (>1/1,000, <1/100): after long treatment posology, systemic absorption can occur with an inhibition of the adrenal function.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via the relevant national regulatory authority pharmacovigilance.

4.9 Overdose

A topical overdose of ciprofloxacin dexamethasone eye drops may be flushed from the eye(s) with lukewarm tap water or drops may be wiped away with a clean tissue.

No toxic effects are to be expected with an ear overdose with this product.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ciprofloxacin: Pharmacotherapeutic Group – Ophthalmological, Other Anti-infective. ATC Code: S01A X13.

Dexamethasone: Pharmacotherapeutic group: Corticosteroids, plain, ATC code: S01 BA01

Mechanism of Action

The bactericidal action of ciprofloxacin results from inhibition of the enzyme, DNA gyrase, which is required for the synthesis of bacterial DNA.

Dexamethasone is a highly potent and long-acting glucocorticoid. It has an approximately 7 times greater anti-inflammatory potency than prednisolone, another commonly prescribed corticosteroid.

Pharmacodynamic Properties

Ciprofloxacin: Pharmacotherapeutic Group – Ophthalmological, Other Anti-infective. ATC Code: S01A X13.

Dexamethasone: Pharmacotherapeutic group: Corticosteroids, plain, ATC code: S01 BA01

CIPROGLAX-D Eye Drops contain the fluoroquinolone, ciprofloxacin. The bactericidal and inhibitory activity of ciprofloxacin against bacteria results from an interference with the DNA gyrase, an enzyme needed by the bacterium for the synthesis of DNA. Thus, the vital information from the bacterial chromosomes cannot be transcribed which causes a breakdown of the bacterial metabolism. Ciprofloxacin has *in vitro* activity against a wide range of Gram-positive and Gram-negative bacteria.

Mechanism of Resistance

Fluoroquinolone resistance, particularly ciprofloxacin, requires significant genetic changes in one or more of five major bacterial mechanisms: a) enzymes for DNA synthesis, b) protecting proteins, c) cell permeability, d) drug efflux, or e) plasmid-mediated aminoglycoside 6'-N-acetyltransferase, AAC (6')-Ib.

Fluoroquinolones, including ciprofloxacin, differ in chemical structure and mode of action from aminoglycosides, β-lactam antibiotics, macrolides, tetracyclines, sulfonamides, trimethoprim, and chloramphenicol. Therefore, organisms resistant to these drugs may be susceptible to ciprofloxacin**.**

Breakpoints

There are no official topical ocular breakpoints for ciprofloxacin and although systemic breakpoints have been used, their relevance to topical therapy is doubtful. The EUCAST clinical MIC breakpoints used for this antibiotic are the following:

Staphylococcus species	S ≤1 mg/l, R ≥1 mg/l
Streptococcus pneumoniae	S ≤0.125 mg/l, R ≥2 mg/l
Haemophilus influenzae	S ≤0.5 mg/l, R ≥0.5 mg/l
Moraxella catarrhalis	S ≤0.5 mg/l, R ≥0.5 mg/l
Pseudomonas aeruginosa	S ≤0.5 mg/l, R ≥1 mg/l

Susceptibility to Ciprofloxacin

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 the agent in at least some types of infections is questionable. The presentation below lists bacterial species recovered from external ocular infections of the eye.

Commonly Susceptible Species

AEROBIC GRAM-POSITIVE MICROORGANISMS

Corynebacterium accolens
Corynebacterium auris
Corynebacterium propinquum
Corynebacterium psudodiphtheriticum
Corynebacterium striatum
Staphylococcus aureus (methicillin-susceptible – MSSA)

Staphylococcus capitis

Staphylococcus epidermidis (methicillin-susceptible – MSSE)

Staphylococcus hominis
Staphylococcus saprophyticus
Staphylococcus warneri
Streptococcus pneumoniae
Streptococcus viridans Group

AEROBIC GRAM-NEGATIVE MICROORGANISMS

Acinetobacter species
Haemophilus influenzae
Moraxella catarrhalis
Pseudomonas aeruginosa
Serratia marcescens

Species for Which Acquired Resistance May Be a Problem

AEROBIC GRAM-POSITIVE MICROORGANISMS

Staphylococcus aureus (methicillin-resistant – MRSA) *Staphylococcus epidermidis* (methicillin-resistant – MRSE) *Staphylococcus lugdunensis*

AEROBIC GRAM-NEGATIVE MICROORGANISMS

None

OTHER MICROORGANISMS

None

Inherently Resistant Organisms

AEROBIC GRAM-POSITIVE MICROORGANISMS

Corynebacterium jeikium

AEROBIC GRAM-NEGATIVE MICROORGANISMS

None

OTHER MICROORGANISMS

None

CIPROGLAX-D Eye Drops also contain dexamethasone, a highly potent and long-acting glucocorticoid. It has an approximately 7 times greater anti-inflammatory potency than prednisolone, another commonly prescribed corticosteroid.

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 that mediate inflammation, e.g. prostaglandins. Corticosteroids also produce a marked, though transient, lymphocytopenia. This depletion is due to redistribution of the cells, with 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 retardepithelial regeneration, diminish post-inflammatory neo-vascularization and reduce the excessive permeability of inflamed capillaries to normal levels.

The actions of corticosteroids, as described above, are exhibited by dexamethasone and they all contribute to its anti-inflammatory effect.

5.2 Pharmacokinetic properties

Ciprofloxacin

Ciprofloxacin in CIPROGLAX-D Eye Drops is rapidly absorbed into the eye following topical ocular administration. Systemic levels are low following topical administration. Plasma levels of ciprofloxacin in human subjects following two drops of 0.3% ciprofloxacin solution every 2 hours for 2 days and then every 4 hours for 5 days ranged from non-quantifiable (<1.0 ng/mL) to 4.7 ng/mL. The mean peak ciprofloxacin plasma level obtained in this study is approximately 450-fold less than that seen following a single oral dose of 250 mg ciprofloxacin. The systemic pharmacokinetic properties of ciprofloxacin have been well studied. Ciprofloxacin widely distributes to tissues of the body. The apparent volume of distribution at steady state is 1.7–5.0 l/kg. Serum protein-binding is 20–40%. The half-life of ciprofloxacin in serum is 3–5 hours. Both ciprofloxacin and its four primary metabolites are excreted in urine and faeces. Renal clearance accounts for approximately two-thirds of the total serum clearance, with biliary and faecal routes accounting for the remaining percentages. In patients with impaired renal function, the elimination half-life of ciprofloxacin is only moderately increased due to extra-renal routes of elimination. Similarly, in patients with severely reduced liver function the elimination half-life is only slightly longer.

There are no pharmacokinetic data available with respect to use in children.

Dexamethasone

Absorption

When administered topically into 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, kidneys 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.

Biotransformation

Dexamethasone 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 ± 0.9 hours.

Elimination

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

5.3 Preclinical safety data

Ciprofloxacin

After topical application of ciprofloxacin 0.3%, (one drop every 30 minutes for a total of six doses), the concentration of ciprofloxacin achieved in the aqueous humour of rabbits when the corneal epithelium was intact was 4.8 µg/mL; when debrided, it was 12.9 µg/mL.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and carcinogenic potential. Non-clinical developmental toxicity was observed only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use.

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 fetal development, including cleft palate, intra-uterine growth retardation and

6. Pharmaceutical Particulars

6.1 List of Excipients

PEG-400	USP
Disodium EDTA	BP
Lactic acid	BP
Benzalkonium chloride solution	BP
Water for injection	BP

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

2 years.
After the first opening of the container, the sterile ophthalmic solution should not be used longer than four weeks.

6.4 Special Precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and Content of container

5 ml sterile white color plastic vial along with the pack insert is packed in Primary Carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Hanuchem Laboratories
1317 – 20, Manpura, Baddi, Dist. Solan (HP.) 173205. India.

8. Marketing Authorization Number

H2022/CTD8878/20478

9. Date of first authorization/renewal of the authorization

5/9/2022

10. Date of revision of the text

5/9/2022