AUSTRALIAN PI – MAXIDEX® (DEXAMETHASONE) EYE DROPS

1 NAME OF THE MEDICINE

Dexamethasone

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Maxidex Eye Drops contain 1 mg/mL dexamethasone and is preserved with benzalkonium chloride (0.1 mg/mL).

May contain potential allergen sulfites from the manufacturing process.

For a full list of excipients see section 6.1 'LIST OF EXCIPIENTS'.

3 PHARMACEUTICAL FORM

The eye drops are a white to pale yellow, opaque suspension with no agglomerates.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe, such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivitis when the inherent hazard of steroid use is accepted to obtain an advisable diminution in oedema and inflammation; corneal injury from chemical radiation or thermal burns or penetration of foreign bodies.

4.2 DOSE AND METHOD OF ADMINISTRATION

One or two drops topically in the conjunctival sac(s). In severe disease, drops may be used hourly, being tapered to discontinuation as the inflammation subsides. In mild disease, drops may be used up to four to six times daily.

Nasolacrimal occlusion or gently closing the eyelid after administration is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic adverse reactions.

Instructions to Patients

Shake bottle well before using.

No contact lenses should be worn under Maxidex Eye Drops treatment (see Section 4.4 Special Warnings and Precautions for Use).

To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle.

If more than 1 topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Ointments should be administered last.

4.3 CONTRAINDICATIONS

Maxidex Eye Drops are contraindicated in epithelial herpes simplex (dendritic keratitis), vaccinia, varicella, and most other viral diseases of the cornea and conjunctiva, tuberculosis of the eye, fungal disease of ocular structures or untreated parasitic eye infections, mycobacterial ocular infections or untreated bacterial eye infections.

Those persons who have shown hypersensitivity to any component of this preparation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Not for injection or oral ingestion

This drug is not effective in the treatment of Sjogren's keratoconjunctivitis. The extensive and/or prolonged use of ophthalmic steroids increases the risk of ocular complications and could cause systemic side effects. If the inflammatory condition does not respond within a reasonable period during the course of the therapy, other forms of therapy should be instituted to reduce these risks.

Prolonged use of ophthalmic steroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, defect in visual acuity and fields of vision, and posterior subcapsular cataract formation. The risk of corticosteroid-induced raised intra-ocular pressure is increased for a patient with a family or personal history of glaucoma or high myopia. If these products are used for 10 days or longer, intraocular pressure should be routinely and frequently monitored even though it may be difficult in children and uncooperative patients. The risk of corticosteroid-induced ocular hypertension may be greater in children and may occur earlier than in adults. Maxidex Eye Drops is not approved for use in paediatric patients. The risk of corticosteroid induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes). Risk-benefit should be considered in a patient with diabetes mellitus as they may be predisposed to an increase in posterior subcapsular cataract formation.

Cushing's syndrome and/or adrenal suppression associated with systemic absorption of ophthalmic 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) see section 4.5 INTERACTIONS WITH OTHER MEDICIENS AND OTHER FORMS OF INTERACTIONS. . In these cases, treatment should not be discontinued abruptly, but progressively tapered.

Corticosteroids may mask infection, reduce resistance to, enhance existing or established bacterial, viral, fungal or parasitic infection. Prolonged use may suppress the immune response and thus increase the hazard of secondary ocular infections. The possibility of persistent fungal infections of the cornea should be considered after prolonged corticosteroid dosing.

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 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.

Ocular herpes simplex has occurred in patients under systemic or local corticosteroid therapy for other conditions. Employment of corticosteroid medication in the treatment of herpes simplex other than

epithelial herpes simplex keratitis, in which it is contraindicated, requires great caution and only in conjunction with antiviral therapy; periodic slit-lamp microscopy is essential.

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

Maxidex Eye Drops contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. In case patients are allowed to wear contact lenses, they must be instructed to remove contact lenses prior to application of Maxidex Eye Drops and wait at least 15 minutes before reinsertion.

Visual Disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Use in hepatic impairment

The safety and efficacy of Maxidex in patients with hepatic impairment has not been established.

Use in renal impairment

The safety and efficacy of Maxidex in patients with renal impairment has not been established.

Use in the elderly

The safety and efficacy of Maxidex in elderly patients have not been established.

Paediatric use

The safety and effectiveness of Maxidex Eye Drops in paediatric patients have not been established. However, increased susceptibility to raised IOP and cataract formation have been described in the literature.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

An additional increase in intraocular pressure cannot be excluded if dexamethasone is used concomitantly with atropine or other anticholinergics which themselves may lead to IOP elevations in predisposed patients.

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

CYP3A4 inhibitors including ritonavir and cobicistat may increase systemic exposure resulting in increased risk of adrenal suppression/Cushing's syndrome. (See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE). 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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Studies have not been performed to evaluate the effect of topical ocular administration of dexamethasone on fertility. There is limited clinical data to evaluate the effect of dexamethasone on male or female fertility. No study has been conducted in animals to investigate the effect of Maxidex Eye Drops on fertility.

Use in pregnancy – Pregnancy Category B3

Reduced placental and birth weights have been recorded in both animals and humans after long-term treatment with corticosteroid.

There are no adequate or well-controlled studies in pregnant women. Currently available clinical data provides no conclusive evidence that corticosteroids caused an increased incidence of congenital abnormalities. Prolonged or repeated use during pregnancy was associated with an increased risk of intra-uterine growth retardation, although this did not appear to be evident following short-term treatment. Topical corticosteroids should not be used extensively in pregnant women in large amounts or for prolonged periods of time. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

Maxidex Eye Drops should not be used in pregnancy unless the potential benefit to the mother outweighs the potential risk to the embryo or foetus.

Use in lactation

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. A risk to the suckling child cannot be excluded. Because many drugs are excreted in milk, caution should be exercised when Maxidex Eye Drops is administered to a nursing woman. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Maxidex Eye Drops 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

Instillation of eye drops may cause transient blurring of vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems

The following adverse events have been reported following use of this or other topical ophthalmic steroid preparations:

Eye Disorders

Rare (≥0.01% < 0.1%): visual acuity reduced, subcapsular cataract, glaucoma, visual field defect, eyelid ptosis, mydriasis.

Infections and Infestations

Rare (≥0.01% < 0.1%): eye infection (exacerbation or secondary).

Injury, Poisoning and Procedural Complications

Very Rare (< 0.01%): corneal perforation.

Investigations

Uncommon (≥0.1% <1%): intraocular pressure increased.

Skin and Subcutaneous Tissue Disorders

Rare (≥0.01% < 0.1%): rash, periorbital oedema.

Post-marketing Events

The following adverse reactions are classified according to the following convention: very common, common, uncommon, rare, very rare, or not known (cannot be estimated from the available data), according to system organ classes. Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions have been observed during clinical trials and post-marketing experience with Maxidex Eye Drops.

Eye disorders

Common (≥ 1% to < 10%): ocular discomfort.

Uncommon (≥ 0.1% to < 1%): keratitis, conjunctivitis, keratoconjunctivitis sicca, corneal staining, photophobia, vision blurred (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE), eye pruritus, foreign body sensation in eyes, lacrimation increased, abnormal sensation in eye, eyelid margin crusting, eye irritation, ocular hyperaemia.

Not Known: glaucoma, ulcerative keratitis, intraocular pressure increased, visual acuity reduced, corneal erosion, eyelid ptosis, eye pain, mydriasis.

Immune system disorders

Not Known: hypersensitivity.

Nervous system disorders

Uncommon (≥ 0.1% to < 1%): dysgeusia.

Not Known: dizziness, headache.

Endocrine disorders

Not Known: Cushing's syndrome, adrenal insufficiency.

4.9 OVERDOSE

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

A topical overdose of Maxidex Eye Drops may be flushed from the eye(s) with tepid water. Accidental ingestion of Maxidex Eye Drops is not likely to be associated with toxicity. Treatment of any overdose is symptomatic and supportive.

If acute overdose is suspected, Maxidex Eye Drops must be ceased immediately and appropriate assessment, monitoring and treatment commenced.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Topical ocular steroid administration has been demonstrated to be effective in the treatment of inflammatory non-infectious diseases of the anterior eye segment, the cornea, and conjunctiva. Systemic administration is however required for the treatment of posterior eye segment disease.

Mechanism of action

Dexamethasone is a 11-hydroxy-16-methyl glucocorticoid fluorinated in the 9α position.

The therapeutic use of dexamethasone is based on its pronounced antiinflammatory activity which is 25 to 30 times higher than that of cortisol while dexamethasone-induced side effects such as retention of sodium and water, loss in potassium and abnormal glucose metabolism are minimal in comparison to cortisol.

The mechanism of action of synthetic steroids is similar to that of cortisol. They bind to specific intracellular receptor proteins. The specific mechanism responsible for the suppression of inflammatory and allergic reactions is not fully understood. Inhibition of the synthesis of specific proteins involved in chemotoxic and immunological processes and other changes in leukocyte and macrophage function appear to be of importance.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

The determination of the ocular availability of dexamethasone after topical ocular administration is based on patients undergoing cataract extraction. The maximum aqueous humor level was reached within 2 hours. The subsequent level decrease resulted in a half-life of 3 hours.

Placental Transfer

Like all corticosteroids, dexamethasone can cross the placenta barrier. This forms the basis for the prophylactic administration of corticosteroids to pregnant women in imminent premature birth to promote fetal lung maturation.

Excretion into Human Milk

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in milk, caution should be exercised when Maxidex Eye Drops is administered to a nursing woman.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Dexamethasone was negative in some bacterial reverse gene mutation assays, but the results are not conclusive and dexamethasone was found to be clastogenic both *in vitro* in human blood lymphocytes and *in vivo* in mice.

Carcinogenicity

No study has been conducted in animals to investigate the carcinogenic potential of Maxidex Eye Drops.

Studies in animals have shown reproductive toxicity. In animal studies, corticosteroids have caused abortion and various types of malformations (cleft palate and multiple skeletal abnormalities). Reduced placental and birth weights have been recorded in both animals and humans after long-term treatment with corticosteroid. The teratogenicity of dexamethasone has also been demonstrated in mice and rabbits following topical ophthalmic application in multiple of the recommended therapeutic dose.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Maxidex Eye Drops contain 1 mg/mL dexamethasone, together with dibasic anhydrous sodium phosphate, polysorbate 80 (Tween 80), disodium edetate, sodium chloride, hypromellose and purified water. Citric acid monohydate and/or sodium hydroxide are used to adjust the pH. The suspension is preserved with benzalkonium chloride (0.1 mg/mL).

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

Discard container 4 weeks after opening.

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25 °C. Do not Freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

The eye drops are supplied in a 5 mL LDPE bottle with a LDPE plug and PP closure.

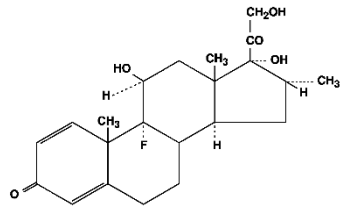
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical name: Pregna-1,4-diene-3,20-dione,9-fluoro-11,17,21-trihydroxy-16-methyl-,(11β,16α)

Chemical structure



Dexamethasone is a white or almost white, crystalline powder, practically insoluble in water, sparingly soluble in ethanol, slightly soluble in methylene chloride. It has a molecular weight of 392.5 and a melting point of 255 °C (with decomposition).

CAS number

50-02-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

15 October 1991

10 DATE OF REVISION

18 November 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
3	Revision of Pharmaceutical form section
6.5	Revision of nature and contents of the container

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