

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. Name of the medicinal product

Dexamethasone 0.1% w/v eye drops, suspension  
Maxidex

### 2. Qualitative and quantitative composition

Dexamethasone 0.1% w/v  
Excipient with known effect in suspension:  
Benzalkonium Chloride 0.01% w/v. See section 4.4.  
For the full list excipients, see section 6.1.

### 3. Pharmaceutical form

White to pale yellow opaque eye drops, suspension.

### 4. Clinical particulars

#### 4.1 Therapeutic indications

Indicated for treatment of steroid responsive inflammatory conditions of the conjunctiva, cornea and anterior segment of the eye, such as, anterior uveitis, iritis, cyclitis, allergic and vernal conjunctivitis, herpes zoster keratitis, superficial punctate keratitis and non-specific superficial keratitis.

Also indicated for the treatment of corneal injury from chemical, radiation or thermal burns or following penetration by foreign bodies. Indicated for post-operative use to reduce inflammatory reactions and suppress graft reaction.

#### 4.2 Posology and method of administration

Adults, adolescents, and children (2 years of age and above)

The frequency of instillation of drops and the duration of treatment will vary depending upon the severity of the underlying condition and the response to treatment.

Severe inflammations require one to two drops instilled into the eye every thirty to sixty minutes until a satisfactory response occurs.

Subconjunctival or systemic steroid therapy should be considered if there is no response. When a favourable response has been observed reduce the dosage towards one drop every four hours.

Method of Administration

For ocular use only.

Shake the bottle well before use.

After cap is removed, if tamper evident snap collar is loose, remove before using product.

Do not let the tip of the dropper touch the eye.

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.

Paediatric patients

The safety and efficacy of this product has not been established in children below 2 years of age.

Hepatic and renal impairment

The safety and efficacy of Maxidex in patients with hepatic or renal impairment have not been established.

#### **4.3 Contraindications**

- Vaccinia, varicella, or other viral diseases of cornea and conjunctiva (except herpes zoster keratitis)
- Herpes simplex keratitis
- Fungal diseases of ocular structures or untreated parasitic eye infections
- Mycobacterial ocular infections
- Acute, untreated bacterial infections
- Hypersensitivity to dexamethasone or to any of the excipients listed in section 6.1.

#### **4.4 Special warnings and precautions for use**

- 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. This is especially important in paediatric patients as the risk of corticosteroid-induced ocular hypertension may be greater in children and may occur earlier than in adults. The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes).
- Topical corticosteroids should not be used for longer than one week except under ophthalmic supervision, with regular checks of intraocular pressure.
- 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.
- Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral, fungal or parasitic infections and mask the clinical signs of infections. In such cases antibiotic therapy is mandatory. Fungal infection should be suspected in patients with persistent corneal ulceration 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. (See section 4.5).
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.
- 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 be cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.
- The wearing of contact lenses is discouraged during treatment of an ocular inflammation.
- There is no evidence of safety in use in children under two years of age.
- In patients receiving systemic corticosteroids, new-onset or exacerbation of pre-existing diabetes mellitus may occur. Because of the possibility of reduced glucose tolerance/diabetes mellitus

with topical ophthalmic corticosteroids, caution is recommended when administering Maxidex to patients with a personal or family history of diabetes.

#### Excipients

Additionally, this product contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. However, if the healthcare provider consider contact lenses use appropriate, patients must be instructed to remove contact lenses prior to application of Maxidex and wait at least 15 minutes before reinsertion.

### **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

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

CYP3A4 inhibitors (including ritonavir 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.

The possibility of a higher need for hypoglycaemic medicinal products must be taken into consideration when administering Maxidex to diabetic patients because the hypoglycaemic effect of these medicinal products may be reduced (see section 4.4).

### **4.6 Pregnancy and lactation**

#### 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.

Dexamethasone had no adverse effects on female fertility in rat model (see section 5.3).

#### Pregnancy

There are no adequate or well-controlled studies evaluating the use of Maxidex in pregnant women. Prolonged or repeated corticoid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism. Studies in animals have shown reproductive toxicity (see section 5.3).

Maxidex is not recommended during pregnancy unless the clinical condition of the woman requires treatment with Maxidex .

#### Lactation

It is unknown whether Maxidex is excreted in human milk. No data is available on the passage of dexamethasone into human breast milk. It is not likely that the amount of dexamethasone in human milk would be capable of producing clinical effects in the infant following maternal use of the product. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Maxidex 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**

Maxidex has no or negligible influence on the ability to drive and use machines. As with any topical ophthalmic medicinal product, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs upon instillation, the patient must wait until the vision clears before driving or using machinery.

#### 4.8 Undesirable effects

##### Summary of the safety profile

In clinical trials, the most common adverse reaction was ocular discomfort.

##### Tabulated list of adverse reactions

The following adverse reactions are classified according to the following convention: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $<1/10$ ), uncommon ( $\geq 1/1,000$  to  $<1/100$ ), rare ( $\geq 1/10,000$  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 post-marketing experience with Maxidex.

<b>System Organ Classification</b>	<b>MedDRA Preferred Term (v. 12.0)</b>
Immune system disorders	<i>Not known:</i> hypersensitivity
Endocrine disorders	<i>Not known:</i> Cushing's syndrome, adrenal suppression (see section 4.4)
Nervous system disorders	<i>Uncommon:</i> dysgeusia <i>Not known:</i> dizziness, headache
Eye disorders	<i>Common:</i> ocular discomfort <i>Uncommon:</i> keratitis, conjunctivitis, dry eye, vital dye staining cornea present, photophobia, vision, blurred (see also section 4.4), eye pruritus, foreign body sensation in eyes, lacrimation increased, abnormal sensation in eyes, eyelid margin crusting, eye irritation, ocular hyperaemia <i>Not known:</i> glaucoma, ulcerative keratitis, intraocular pressure increased, visual acuity reduced, corneal erosion, eyelid ptosis, eye pain, mydriasis

##### Description of selected adverse reactions

Prolonged topical ophthalmic corticosteroids may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects, and to posterior subcapsular cataract formation (see section 4.4).

Due to the corticosteroid component, in diseases causing thinning of the cornea or sclera there is a higher risk for perforation especially after long treatments (see section 4.4).

Corticosteroids may reduce resistance to and aid in the establishment of infections (see section 4.4).

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

Corticosteroids may impair glucose tolerance, which can lead to new-onset or exacerbation of diabetes mellitus (see section 4.4).

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the Medicines Control Authority of Zimbabwe website: [www.mcaz.co.zw](http://www.mcaz.co.zw).

### **4.9 Overdose**

Long-term intensive topical use may lead to systemic effects. Oral ingestion of the contents of the bottle (up to 10 mls) is unlikely to lead to any serious adverse effects.

An ocular overdose of Maxidex can be flushed from the eye(s) with lukewarm water.

## **5. Pharmacological properties**

### **5.1 Pharmacodynamic properties**

Pharmacological Classification: 19.2.1 Ophthalmic Corticosteroids without Antibiotics

Dexamethasone has been demonstrated by animal and human studies based on oral application to possess approximately six to seven times the potency of prednisolone and at least 30 times the potency of cortisone. The potency of the compound is accomplished by the addition of a methyl radical and a fluorine atom to the prednisolone radical.

### **5.2 Pharmacokinetic properties**

Dexamethasone is absorbed rapidly after oral administration with a half-life of about 190 minutes. Sufficient absorption may occur after topical application to the skin and eye to produce systemic effects. In plasma dexamethasone protein binding is less than for most other corticosteroids. Corticosteroids diffuse into tissue fluids and cerebrospinal fluid but transplacental diffusion in significant amounts has not been demonstrated. Corticosteroids are metabolised in the liver the kidney and excrete in the urine. Metabolism is similar to other corticosteroids. Intraocular penetration occurs in significant amounts and contributes to the effectiveness of dexamethasone in anterior segment inflammatory disease.

### **5.3 Preclinical safety data**

Repeat dose topical ocular safety studies with dexamethasone in rabbits have shown systemic corticosteroid effects. Such effects are considered to be unlikely when Maxidex is 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 Maxidex 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 effects on brain growth and development. The ocular administration of 0.1% dexamethasone also resulted in fetal anomalies in rabbits. Dexamethasone had no adverse effects on female fertility in a chorionic gonadotropin primed rat model.

There are no other preclinical data of relevance to the prescriber which are additional to that included in other sections of the SPC.

## **6. Pharmaceutical particulars**

### **6.1 List of excipients**

Sodium phosphate  
Polysorbate 80  
Disodium edetate  
Sodium chloride  
Benzalkonium chloride  
Hypromellose  
Citric acid  
Purified water

### **6.2 Incompatibilities**

None known.

### **6.3 Shelf life**

24 months (unopened), 1 month (after first opening).

### **6.4 Special precautions for storage**

Do not store above 30°C.  
Do not refrigerate or freeze.  
Keep container tightly closed.  
Discard 1 month after first opening.  
Store in the original package.

### **6.5 Nature and contents of container**

Drop-Tainer - 5ml and 10ml Natural Low Density Polyethylene Bottles and Plugs.  
Polystyrene or Polypropylene cap.

### **6.6 Special precautions for disposal and other handling**

Do not touch dropper tip to any surface as this may contaminate the contents.  
If the drop of medication is not retained in the eye upon dosing for any reason then instill another drop.

**7. Applicant**

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**8. Manufacturer**

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**9. Registration Details**

Zimbabwe registration number: 98/19.2.1/3364  
Zimbabwe Category for Distribution: Prescription Preparations (P.P.)

**10. Date of revision of the text**

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