Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Maxidex 0.1% w/v Eye Drops, Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dexamethasone 0.1% w/v.

Excipients with known effect in suspension:
0.01% w/v Benzalkonium Chloride,
6.5 mg of phosphates in 5 ml, which is equivalent to 1.3 mg/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, suspension
Whitish suspension, free from flocculates.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Indicated for the treatment of allergic and inflammatory conditions of the eye.

4.2 Posology and method of administration

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

One drop instilled into the conjunctival sac every 30-60 minutes for 3-4 days or until a satisfactory response occurs.

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 for 2 minutes 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 of this product has not been established in children below 2 years of age.

Elderly population
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

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

4.3 Contraindications

- Ocular viral infections such as vaccinia, varicella

- Herpes simplex keratitis.
- Fungal disease of ocular structures or untreated parasitic eye infections and 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 and 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.
- Corticosteroid usage may reduce resistance to and aid in the establishment of bacterial, viral, fungal or parasitic infections and mask the clinical signs of infections, preventing recognition of ineffectiveness of the antibiotic. 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. (See section 4.5).
- Topical steroids may induce corneal perforation. Topical steroids may lead to perforation if used in the presence of diseases causing thinning of the cornea or sclera.
- Use with great caution, and only in conjunction with antiviral therapy, in the treatment of stromal keratitis or uveitis caused by herpes simplex; periodic slit-lamp microscopy is essential.
- 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.

- There is no evidence of safety in use in children under two years of age.
- The wearing of contact lenses is discouraged during treatment of an ocular inflammation.
- 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 considers 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.
- This medicine contains 6.5mg of phosphates in each 5 ml respectively, which is equivalent to 1.3mg/ml. If you suffer from severe damage to the clear layer at the front of the eye (the cornea) phosphates may cause in very rare cases cloudy patches on the cornea due to calcium build-up during treatment.

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.

4.6 Fertility, 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 was free of adverse effects on fertility in a chorionic gonadotropin primed rat model.

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 after systemic administration. The ocular administration of 0.1% dexamethasone also resulted in fetal anomalies in rabbits (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 would be detectable in human milk or 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 (≥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 post-marketing experience with Maxidex.

System Organ Classification	**MedDRA Preferred Term (v. 18.1)**
Immune system disorders	*Not known:* hypersensitivity
Endocrine disorders	*Not known:* Cushing's syndrome, adrenal suppression (see section 4.4)
Nervous system disorders	*Uncommon:* dysgeusia *Not known:* dizziness, headache
Eye disorders	*Common:* ocular discomfort *Uncommon:* 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 *Not known:* 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.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Long-term intensive topical use may lead to systemic effects. Oral ingestion of the contents of the bottle (up to 10 ml) 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

Pharmacotherapeutic Group - Ophthalmologicals: Anti-inflammatory Agents.
ATC Code S01B A01.

Dexamethasone is a synthetic glucocorticoid with a potent anti-inflammatory activity. The relative anti-inflammatory potency of dexamethasone is 25 times that of cortisone, but its effects on sodium and water retention, potassium loss and abnormal sugar metabolism are minimal.

5.2 Pharmacokinetic properties

Dexamethasone, like other corticosteroids, is absorbed rapidly after oral administration and has a biological half-life ofabout 190 minutes. Sufficient absorption may occur after topical application to the skin and eye to produce systemic effects. Intraocular penetration of dexamethasone 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 foetal development including cleft palate, intra-uterine growth retardation and affects on brain growth and development.

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

Disodium phosphate
Polysorbate 80
Disodium edetate
Sodium chloride
Benzalkonium chloride
Hypromellose
Citric acid monohydrate (for pH adjustment)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: 20 months
Once opened: Discard one month after first opening.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze. Keep container tightly closed.
Store in the original package.

6.5 Nature and contents of container

Natural low density polyethylene (LDPE) bottle with a natural LDPE dispensing plug and white polypropylene closure containing 5 ml or 10 ml suspension.

Tamper evidence is provided by a closure with extended skirt that breaks away from the closure on opening.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Shake well before use.

7 MARKETING AUTHORISATION HOLDER

Novartis Ireland Limited
Vista Building
Elm Park
Merrion Road, Ballsbridge
Dublin 4
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0896/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 January 1984

Date of last renewal: 05 January 2008

10 DATE OF REVISION OF THE TEXT