Summary of Product Characteristics

MAXIDEX® (dexamethasone)
1 mg/mL, Eye drops, suspension and solution
and 1 mg/g Eye ointment

1 Tradename(s)

MAXIDEX® 1 mg/mL eye drops, suspension and 1mg/g Ointment.

2 Qualitative and quantitative composition

Active substance(s)

Maxidex 1 mg/mL Eye drops, suspension/solution

1 mL of suspension/solution contains 1 mg of dexamethasone

Maxidex 1 mg/g Eye ointment

1 g of ointment contains 1 mg of dexamethasone.

Excipients

Maxidex 1 mg/mL Eye drops, suspension/solution

Excipient with known effect: 1 mL of eye drop suspension contains 0.04 mg of benzalkonium chloride.

For full list of excipients, see section 6.1

3 Pharmaceutical form(s)

Eye drops, suspension/solution

Eye ointment Maxidex 1 mg/mL Eye drops, suspension/solution

White or colourless to pale yellow, clear solution/opaque suspension, without agglomerates.

Maxidex 1 mg/g Eye ointment

Colourless or white or off-white to light yellow homogeneous ointment.

Maxidex 1 mg/g Eye ointment

Excipients with known effect: methylparahydroxybenzoate and propylparahydroxybenzoate.

Other excipients: Anhydrous liquid lanolin and White petrolatum (soft paraffin).

4 Clinical particulars

4.1 Therapeutic indications

Maxidex is indicated in adults for the symptomatic relief of corticosteroid-responsive allergic and inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe, such as allergic or vernal conjunctivitis, acne rosacea keratitis, superficial punctate keratitis, herpes zoster keratitis, uveitis, iritis, and cyclitis, selected infective conjunctivitides 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 Posology and method of administration

Dosage regimen

Maxidex 1 mg/mL Eye drops, suspension/solution

- Topical application (1 or 2 drops in the conjunctival sac).
- For severe or acute inflammation: drops may be used every 30 to 60 minutes as initial therapy, being tapered to discontinuation as inflammation subsides.
- For chronic inflammation: drops may be used every 3 to 6 hours, or as frequently as necessary, being tapered to discontinuation as inflammation subsides.
- Allergies or minor inflammation: drops may be used every 3 to 4 hours until the desired response is obtained, being tapered to discontinuation as inflammation subsides. Prolonged treatment over several days should only be carried out under medical supervision.

Maxidex 1 mg/g Eye ointment

- Apply ribbon of ointment into the conjunctival sac(s) up to 4 times daily. When a favorable response is observed, dosage may be reduced gradually to once a day application for several days.

Special populations

Renal and hepatic impairment

No studies have been performed in patients with renal or hepatic impairment. No dosage regimen adjustment is required for patients with renal impairment.

Pediatric patients (below 18 years)

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

Geriatric patients (65 years of age or above)

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

Method of administration

- For ocular use only.
- After cap is removed, if tamper evident snap collar is loose, it should be removed before using the product.
- Do not let the tip of the tube/dropper touch the eye.
- 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.

Maxidex 1 mg/mL Eye drops, suspension/solution

- Shake the bottle well before use.
- Nasolacrimal occlusion or gently closing the eyelid(s) after administration is recommended. This may reduce the systemic absorption of medicinal products administered via ocular route and result in a decrease in systemic adverse reactions.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Acute, untreated bacterial infections
- Herpes simplex keratitis
- Vaccinia, varicella, and other viral infections of cornea or conjunctiva
- Fungal diseases of ocular structures or untreated parasitic eye infections
- Mycobacterial ocular infections

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 should be checked routinely and frequently. The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g., diabetes).
- 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). In these cases, treatment should not be discontinued abruptly, but progressively tapered.
- Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral, fungal, or parasitic infections and mask the clinical signs of infection.
- Fungal infection should be suspected in patients with persistent corneal ulceration. 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.
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.
- The wearing of contact lenses is discouraged during treatment of an ocular inflammation.

Special excipients

Maxidex 1 mg/mL Eye drops, suspension/solution

- Maxidex Eye Drops contains benzalkonium chloride which may cause eye irritation and may possibly discolor soft contact lenses. Contact lenses must be removed before administration ofMaxidex Eye drops and reinserted at least 15 minutes later.

Maxidex 1 mg/g Eye ointment

- Maxidex Eye ointment contains methylparahydroxybenzoate and propylparahydroxybenzoate, which may cause allergic reactions (possibly delayed).

4.5 Interactions with other pharmaceutical products and other forms of interactions

- 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 of dexamethasone resulting in increased risk of adrenal suppression/Cushing's syndrome (see section 6 Warnings and precautions). 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 Pregnancy, lactation, females and males of reproductive potential

Pregnancy

Risk summary

There are no adequate and well-controlled studies with Maxidex in pregnant women to inform a product-associated risk.

Prolonged or repeated corticosteriod 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.

Maxidex Eye drops/ointment is not recommended during pregnancy.

Lactation

Risk summary

It is not known if dexamethasone is transferred into human milk after administration of Maxidex. 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 or on milk production following maternal use of the product.

A risk to the breastfed child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Females and males of reproductive potential

Infertility

There are no data regarding the effects of topical ocular administration of Maxidex on human or animal fertility. There is limited clinical data to evaluate the effect of dexamethasone on male or female fertility.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Tabulated summary of adverse drug reactions from clinical trials

Adverse drug reactions from clinical trials (Table 4-1) are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention (CIOMS III): 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).

Table 4-1 Adverse drug reactions in clinical trials

System organ classification	Adverse drug reaction	Frequency category
Nervous system orders	Dysgeusia	uncommon
Eye disorders	Ocular discomfort	common
	Keratitis, conjunctivitis, dry eye, vital dye staining cornea present, photophobia, vision blurred, eye pruritus, foreign body sensation in eyes, lacrimation increased, abnormal sensation in eye, eyelid margin crusting, eye irritation, ocular hyperaemia	uncommon

Adverse drug reactions from spontaneous reports and literature cases (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with Maxidex via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. Adverse drug reactions are listed according to system organ classes in MedDRA. Within each system organ class, ADRs are presented in order of decreasing seriousness .

Table 4-2 Adverse drug reactions from spontaneous reports and literature (frequency not known)

System organ classification	Adverse drug reaction	Frequency category
Nervous system disorders	Dizziness, headache	Not known
Immune system disorders	Hypersensitivity	Not known

Endocrine disorders	Cushing's syndrome, adrenal insufficiency	Not known
Eye disorders	Glaucoma, ulcerative keratitis, intraocular pressure increased, visual acuity reduced, corneal erosion, eyelid ptosis, eye pain, mydriasis	Not known

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 Pharmacy and Poisons Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdosage

Due to the characteristics of this preparation, no additional toxic effects are to be expected with an acute ocular overdose of this product or in the event of accidental ingestion of the contents of one bottle or tube.

A topical overdose of Maxidex Eye drops/ointment can be flushed from the eye(s) with lukewarm water

5 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group, ATC

Pharmacotherapeutic group: corticosteroids. ATC code: S01BA01

Mechanism of action (MOA)

The exact mechanism of anti-inflammatory action of dexamethasone is unknown. It inhibits multiple inflammatory cytokines and produces multiple glucocorticoid and mineralocorticoid effects. Dexamethasone is one of the most potent corticosteroids; with a relative anti-inflammatory potency greater than prednisolone or hydrocortisone.

5.2 Pharmacokinetic properties

Absorption

After topical ocular administration, dexamethasone is detectable after 30 minutes in the aqueous humor and peaks at 90 to 120 minutes with a mean concentration of 31 ng/mL. Low but detectable concentrations are observed in the aqueous humor after 12 hours. Oral bioavailability of dexamethasone ranged from 70%-80% in normal subjects and patients.

Distribution

After intravenous administration, the volume of distribution at steady state was 0.58 L/kg. *In vitro*, no change in human plasma protein binding was observed with dexamethasone

concentrations from 0.04 to 4 μg/mL, with a mean plasma protein binding of 77.4%.

Biotransformation/metabolism

After oral administration, two major metabolites were recovered which 60% of the dose was recovered as 6β-hydroxydexamethasone and up to 10% recovered as 6β-hydroxy-20-dihydrodexamethasone.

Elimination

After intravenous administration, the systemic clearance was 0.125 L/hr/kg. After i.v. bolus administration, 2.6% of the unchanged parent drug was recovered in the urine while up to 70% of the dose was recovered as identified metabolites. After systemic dosing, the half-life has been reported as 3-4 hours but was found to be slightly longer in males. This observed difference was not attributed to changes in systemic clearance but to differences in volume of distribution and body weight.

Linearity/non-linearity

Linear pharmacokinetics was observed after oral administration with doses between 0.5 to 1.5 mg where the AUC was less than proportional to the oral dose.

Special populations

Pharmacokinetics of systemic dexamethasone did not significantly differ in renal-impaired patients when compared to normal subjects.

Pediatric pharmacokinetics varied between age groups but wide interpatient variabilities were observed. The safety and efficacy of dexamethasone suspension/ointment have not been studied in children; however, dexamethasone is reportedly safe for pediatric use, in general.

5.3 Pre-clinical safety data

Non-clinical data reveal no special hazard for humans, at the recommended clinical dose, based on conventional studies of repeated dose toxicity, genotoxicity, or carcinogenic potential.

For reproductive toxicity, see Section 9 Pregnancy, lactation and females and males of reproductive potential

6 Pharmaceutical information

6.1 List of excipients

Other excipients: sodium chloride, hypromellose (hydroxypropylmethylcellulose), disodium phosphate, polysorbate 80, disodium edetate (EDTA), citric acid monohydrate and/or sodium hydroxide (to adjust pH) and Purified Water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Maxidex 1 mg/mL Eye drops, suspension/solution

Store the bottle upright. Keep the bottle tightly closed.

Store protected from light (in the original carton).

Maxidex 1 mg/g Eye ointment

Do not refrigerate or freeze. Keep the tube tightly closed.

Maxidex Eye drops, suspension/solution and ointment must be kept out of the sight and reach of children.

6.5 Nature and contents of container

Maxidex 1 mg/mL Eye drops, suspension/solution

5ml solution in a LDPE plastic bottle

Maxidex 1 mg/g Eye ointment

3.5g of ointment in LDPE/AL-HDPE tube

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 Marketing authorization holder and manufacturing site address

Novartis Pharma AG

Lichtstrasse 35,

CH-4056 Basel,

Switzerland

Manufacturer

Novartis Manufacturing NV

Rijksweg 14,

2870 Puurs-Sint-Amands

Belgium

8 Marketing authorization number

Maxidex 1 mg/mL Eye drops, suspension/solution: 1266

Maxidex 1 mg/g Eye ointment: 1282

9 Date of first registration/ renewal of the registration

Kenya: 16 Jan 1984

10 Date of revision of the text

July 2023.