1 NAME OF THE MEDICINAL PRODUCT

MAXIDEX 1 mg/ml eye drops, suspension

MAXIDEX 1 mg/g, eye ointment

Isopto®-Maxidex 1 mg/ml eye drops, suspension

MAXIDEX, eye drops, suspension 0.1% w/v

MAXIDEX 0.1% w/v, eye drops, suspension

THILODEXINE eye drops, solution 0.1% w/v

Maxidex

Maxidex Eye Drops

Maxidex suspension

MAXIDEX EYE DROPS, SUSPENSION

MAXIDEX 0.1% w/w Eye Ointment

Isopto-Maxidex 1 mg/ml eye drops, suspension

Dexa-sine eye drops, solution

**Alternative names may be applicable. Refer to the currently approved local product labeling.*

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL of suspension/solution contains 1 mg of dexamethasone or 1 mg dexamethasone sodium phosphate

1 g of ointment contains 1 mg of dexamethasone.

Excipient with known effect in solution/suspension: benzalkonium chloride 0.1 mg/ml.

Excipients with known effect in ointment: methylparahydroxybenzoate and propylparahydroxybenzoate.

For the full list of excipients, see section 6.1.

**Information might differ in some countries. Refer to the currently approved local product labeling.*

3 PHARMACEUTICAL FORM

Eye drops, suspension/solution

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

Eye ointment

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

**Information might differ in some countries. Refer to the currently approved local product labeling.*

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Corticosteroids are applied topically to the conjunctiva 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. [1]

**Refer to the currently approved product labeling. Indication and patient population as per national approval.*

4.2 Posology and Method of Administration

Posology

Dexamethasone Suspension/Solution [1]

- Topical application (1 or 2 drops in the conjunctival sac).
- SEVERE OR ACUTE INFLAMMATION: Every 30 to 60 minutes as initial therapy, being tapered to discontinuation as inflammation subsides.
- CHRONIC INFLAMMATION: Every 3 to 6 hours, or as frequently as necessary. Being tapered to discontinuation as inflammation subsides.
- ALLERGIES OR MINOR INFLAMMATION: 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.

Dexamethasone Ointment [1]

- 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.

Method of Administration [1]

For ocular use only.

Shake the bottle well before use [*dexamethasone suspension*].

After cap is removed, if tamper evident snap collar is loose, remove before using product *[Only applicable for eye drops containing a snap collar]*.

Do not let the tip of the tube/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 [*dexamethasone suspension*].

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.

Special populations:

Pediatric population [1]

- The safety and efficacy of [dexamethasone ophthalmic suspension/ointment] in children have not been established

Geriatric population [1]

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

Hepatic and renal impairment [1]

- The safety and efficacy of [dexamethasone ophthalmic suspension/ointment] in patients with hepatic or renal impairment have not been established.

Refer to the currently approved product labeling. Posology and patient population as per national approval.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients. [1]
- Acute, untreated bacterial infections. [1]
- Herpes simplex keratitis. [1]
- Vaccinia, varicella, and other viral infections of cornea or conjunctiva. [1]
- Fungal diseases of ocular structures or untreated parasitic eye infections. [1]
- Mycobacterial ocular infections. [1]

4.4 Special Warnings and Precautions for Use

- 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 [dexamethasone suspension]. [1] *[Statement to be included under Section 4.2]*

- 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. *[FOR COUNTRIES THAT HAVE PEDIATRIC USE INCLUDED OR APPROVED IN THE LOCAL LABEL:]* <This is especially important in pediatric patients, as the risk of corticosteroid-induced ocular hypertension may be greater in

children and may occur earlier than in adults.> *[FOR COUNTRIES THAT HAVE PEDIATRIC USE EXCLUDED OR CONTRA-INDICATED IN THE LOCAL LABEL:]* <This is especially important in pediatric patients, as the risk of corticosteroid-induced ocular hypertension may be greater in children and may occur earlier than in adults. *[TRADENAME]* is not approved for use in pediatric patients. The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes). [1]

- 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). In these cases, treatment should not be discontinued abruptly, but progressively tapered. [1],[2]

- Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral, fungal, or parasitic infections and mask the clinical signs of infection. [1]

- Fungal infection should be suspected in patients with persistent corneal ulceration. Corticosteroids therapy should be discontinued if fungal infection occurs. [1]

- 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). [1]

- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids. [1]

- The wearing of contact lenses is discouraged during treatment of an ocular inflammation. [Dexamethasone Eye Drops/Ointment] contains benzalkonium chloride which may cause eye irritation and is known to discolor 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

[Dexamethasone Eye Drops/ Ointment] and wait at least 15 minutes before reinsertion. [Only applicable to products containing benzalkonium chloride] [1]

- This product contains methylparahydroxybenzoate and propylparahydroxybenzoate which may cause allergic reactions (possibly delayed). [Only applicable to products containing methylparahydroxybenzoate and propylparahydroxybenzoate] [1]

4.5 Interaction with other Medicinal Products and Other Forms of Interaction

- Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems. [1]

- CYP3A4 inhibitors including ritonavir and cobicistat may increase systemic exposure resulting in increased risk of adrenal suppression/Cushing's syndrome. (See Section 4.4). 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. [2]

4.6 Pregnancy and Lactation

Fertility [1]

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 [1]

There are no adequate or well-controlled studies evaluating Dexamethasone Eye Drops/ Ointment 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 (See Section 4.4). 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).

[Dexamethasone Eye drops/Ointment] is not recommended during pregnancy.

Lactation [1]

It is unknown whether [Dexamethasone Eye Drops/ Ointment] 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 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.

4.7 Effects on Ability to Drive and Use Machines

Temporary blurred 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. [1]

4.8 Undesirable Effects

The following adverse reactions have been reported during clinical trials with [Dexamethasone Eye Drops/Ointment] and are classified according to the subsequent 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). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness. [1]

System Organ Classification	MedDRA Preferred Term

Nervous system disorders	*Uncommon:* dysgeusia
Eye disorders	*Common:* ocular discomfort *Uncommon:* 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

Additional adverse reactions identified from post-marketing surveillance include the following. Frequencies cannot be estimated from the available data. Within each System Organ Class adverse reactions are presented in order of decreasing seriousness. [1]

System Organ Classification	**MedDRA Preferred Term**
Immune system disorders	*Not known:* hypersensitivity
Endocrine disorders	*Not known:* Cushing's syndrome, adrenal insufficiency
Nervous system disorders	*Not known:* dizziness, headache
Eye disorders	*Not known:* glaucoma, ulcerative keratitis, intraocular pressure increased, visual acuity reduced, corneal erosion, eyelid ptosis, eye pain, mydriasis

4.9 Overdose

- A topical overdose of [Dexamethasone Eye Drops/ Ointment] can be flushed from the eye(s) with lukewarm water. [1]
- 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. [1]

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: corticosteroids. ATC code: S01BA01 [1]

Mechanism of action [1]

The exact mechanism of anti-inflammatory action of dexamethasone is unknown. It inhibits multiple inflammatory cytokines and produces multiple glucocorticoid and mineralocorticoid effects

Pharmacodynamic effects [1]

Dexamethasone is one of the most potent corticosteroids; with a relative anti-inflammatory potency greater than prednisolone or hydrocortisone.

Clinical efficacy and safety [1]

The safety and efficacy of dexamethasone suspension/ointment have been established in adult clinical trials, published literature, and post-marketing surveillance.

Pediatric population [1]

The safety and efficacy of dexamethasone suspension/ointment have not been studied in children; however, dexamethasone is reportedly safe for pediatric use, in general.

5.2 Pharmacokinetic Properties

Absorption [1]

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 [1]

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 [1]

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 [1]

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 [1]

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.

Pharmacokinetic/pharmacodynamic relationship(s) [1]

A pharmacodynamic/pharmacokinetic relationship after topical ocular administration has not been established.

Special Population Pharmacokinetics [1]

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.

5.3 Preclinical 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, carcinogenic potential, or toxicity to reproduction and development. [1]

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Suspension/Solution:

Dibasic sodium phosphate (anhydrous)
Dibasic sodium phosphate dihydrate
Disodium phosphate dodecahydrate
Monobasic disodium phosphate
Polysorbate 80
Disodium edetate (EDTA)
Povidone
Boric acid
Sodium chloride
Benzalkonium chloride
Hypromellose (hydroxypropylmethylcellulose)
Citric acid monohydrate and/or sodium hydroxide (to adjust pH)
Purified water

Ointment:

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Anhydrous liquid lanolin
White petrolatum (soft paraffin)
Cholesterol

**Information might differ in some countries or between products. Refer to the currently approved local product labeling.*

6.2 Incompatibilities

Suspension/Solution:
For information on the use of this product with contact lenses see Section 4.4 Special warning and precautions for use.

Ointment:

Not applicable.

**Refer to the currently approved local product labeling.*

6.3 Shelf Life

Suspension/Solution:

Unopened up to 3 years/36 months.

Discard 28 days after first opening.

Ointment:

Up to 4 years/48 months

Discard 28 days after first opening.

**Information might differ in some countries or for different fill sizes/presentations. Refer to the currently approved local product labeling.*

6.4 Special Precautions for Storage

Suspension/Solution:

No special storage conditions.

Store the bottle upright.

Keep the bottle tightly closed.

Store protected from light (in the original carton).

Ointment:

Do not store above 27°C.

Do not refrigerate or freeze.

Keep the tube tightly closed.

**Information might differ/be more restricted in some countries, depending on local requirements and/or climate zone classification. Refer to the currently approved local product labeling.*

6.5 Nature and Contents of Container

Solution/suspension:

Low density polyethylene (LDPE) bottle with LDPE dropper and polypropylene (PP) tamper-evident cap.

OR

Dropper container (DROPTAINER®- LDPE) with PP screw cap.

The following pack sizes are available: 1 X 5 mL, 1 X 3 mL, 1 X 10 mL, 1 X 15 mL

Not all pack sizes may be marketed.

Ointment:

Epoxy-phenolic aluminum tube with a polyethylene nozzle and closure

OR

3.5g collapsible tin tube with an ophthalmic dispensing nozzle and HDPE screw cap.

The following pack sizes are available: 1 X 3.5 g tube.

Not all pack sizes may be marketed.

**Refer to the currently approved local product labeling. Information might differ in some countries.*

6.6 Instructions for Use and Handling <and Disposal>

No special requirements.

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

**Refer to the currently approved local product labeling. Information might differ in some countries.*

7 CHANGES FROM PREVIOUS VERSION

CDS Amendment- TDOC-0051104 v. 2.0, standard implementation:

The following safety labeling changes have been made to sections 4.4 and 4.5. [Deletion in strikethrough and new information has been underlined.]

- **Section 4.4:** 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). In these cases, treatment should not be discontinued abruptly, but progressively tapered.

- **Section 4.5:** ~~In patients treated with ritonavir, plasma concentrations of dexamethasone may be increased *(See Section 4.4).*~~ CYP3A4 inhibitors including ritonavir and cobicistat may increase systemic exposure resulting in increased risk of adrenal suppression/Cushing's syndrome. (See Section 4.4). 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.

- **Section 5.2:** The following statements have been updated:

Elimination [1]

After intravenous administration, the systemic clearance was 0.125 L/hr/kg. After ~~oral~~ 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 [1]

~~Non-l~~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.

TDOC-0051104 v. 1.0: CCDS Update: This CCDS supersedes TDOC- 0018163.

New TDOC number [TDOC-0051104] that has been created for this CCDS and this is due to the migration and update of Alcon's document management system. This system does not allow versioning up of documents that were created in the older system and this means that in the new system, the migrated document will show as version one, independent of the previous version number. The correct versioning is referenced in the section describing changes since previous version.

- The whole document has been adapted to current CCSI/CCDS templates/standards.
- Section 4.1 has been updated to remove reference to regional approvals and present the company position on efficacy.
- Section 4.2 and relevant justification have been re-written for clarity. Information on Benzalkonium chloride has been included under section 4.4 and removed from this section.
- Section 4.3:
    - Contraindication on Fungal diseases of ocular structures modified to include "or untreated parasitic eye infections".
- Section 4.4:
    - The statement "Nasolacrimal occlusion of 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" has been incorporated as minimum safety information.

    - The warning "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 ritonavir (See Section 4.5). In these cases, treatment should not be discontinued abruptly, but progressively tapered" is added.

    - Warning on resistance to infections updated to include "or parasitic infections".
    - The statement "the warning of contact lenses is discouraged during treatment of an ocular inflammation" is added. The statement "In case patients are allowed to wear contact lenses, they must be instructed to remove contact lenses…" modified

to “However, if the healthcare provider considers contact lenses use appropriate, patients must be instructed to remove contact lenses…”

- Section 4.5:
    - The statement “In patients treated with ritonavir, plasma concentrations of dexamethasone may be increased (See Section 4.4).” is added.
- Section 4.6:
    - The fertility statement is added: “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”
    - The pregnancy statement is modified to: “There are no adequate or well-controlled studies evaluating [Dexamethasone Eye Drops/ Ointment] 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 (See Section 4.4). 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 Preclinical safety data). [Dexamethasone Eye drops/Ointment] is not recommended during pregnancy. *”
    - The breast-feeding statement is modified to: “It is unknown whether [Dexamethasone Eye Drops/ Ointment] 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 therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.*”
- Section 4.8:

Clinical Trials:

- The terms “keratoconjuctivitis sicca” and “corneal staining“ have been recoded to “dry eye” and “vital dye staining cornea present”, respectively.
- No new clinical trials data have been incorporated. List of clinical studies excluded from the CCDS is added.
- Errors in patient numbers and study numbers have been corrected. Incidences of ADRs have been adjusted accordingly.

Post-Marketing Surveillance:

- The section has been updated following the review of Post-Marketing Surveillance data: Cushing’s syndrome, adrenal insufficiency, glaucoma, and ulcerative keratitis have been included in the CCDS.

- Section 4.9:
  - The statement “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” is added.
- Section 5.1 has been updated to provide concise information on corticosteroids. The justification has been updated and re-written for clarity

- Section 5.2:
  Sub-sections have been re-worded. Sub-sections on Linearity/non-linearity, PK/PD Pharmacodynamic relationship and Special population pharmacokinetics have been included.
- Section 5.3 has been amended as follows:
- ~~In comparison to clinically relevant doses, n~~Non-clinical data reveal no special hazard for humans, at the recommended clinical dose, based on conventional studies of ~~safety pharmacology,~~repeated dose toxicity, genotoxicity, carcinogenic potential, or toxicity to reproduction and development. Justification for this section has been re-written for clarity.

New CCDS.

The following changes were made to the previous reference document CCSI (TDOC-0011449, version.4.0):

TDOC-0011449, 4.0 January 2014:

- Section 4.4:
    - The warning “The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes)” was added.
    - The warning “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)” was added.
- Section 4.5:
    - The statement “Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems.” was added and the statement “No clinically relevant interactions have been described” was removed.

TDOC-0011449 v.3.0 March 2013:

- Section 4.4: added warning on the greater risk of corticosteroid-induced ocular hypertension in children.

TDOC-0011449 v.2.0 June 2012:

- Statements aligned with the current QRD and CCSI templates.
- Information restricted to core safety data. Information not considered minimum safety data or not properly justified removed from the document.
- Document amended to be in line with the known safety data on corticosteroids. The following sections updated under this premise:
    - Section 4.3:

        - "Acute untreated purulent bacterial infections" modified to "Acute untreated bacterial infections".
        - "Acute epithelial herpes simplex keratitis" modified to "Herpes simplex keratitis".
        - "Vaccinia varicella and other viral infections of cornea and conjunctiva (except herpes zoster keratitis)" modified to exclude exception.
    - Section 4.4:
        - Warning on resistance to infections updated to exclude text "preventing recognition of ineffectiveness of the antibiotic".
        - Warning on fungal infection updated to delete text "who have been or are receiving these drugs".
        - Warning on stromal keratitis or uveitis caused by herpes simplex has been deleted.
- Additional changes:
    - Section 4.4: Warning against contact lens wear deleted as this is not included per current CCSI standards.

TDOC-0011449 v.1.0 May 2010:

Not applicable. New CCSI.

8 APPENDICES

Not applicable.

9 REFERENCES

1) CCDS Supporting Document (TDOC-0051106 v.1.0). This is the supporting document for the previous CCDS version (TDOC-0051104 v.1.0).

2) Clinical Overview (CO) (TDOC-0054749): Changes to Core Data Sheet (CDS) / Product Information for Dexamethasone and Dexamethasone-containing products.