Summary of Product Characteristics

ONATOB-DEX EYE DROPS

(Tobramycin 3 mg/mL and dexamethasone 1 mg/mL eye drops, solution)

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1. Name of the medicinal product

ONATOB-DEX Eye Drops (Tobramycin and Dexamethasone Eye Drops, Solution)

2. Qualitative and quantitative composition

Each mL of solution contains tobramycin sulfate USP equivalent to tobramycin 3 mg (0.3% w/v) and dexamethasone sodium phosphate USP equivalent to dexamethasone 1 mg (0.1% w/v).

Excipient with known effect:

This medicine contains benzalkonium chloride (to be confirmed from the applicant's formulation; see section 6.1).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Eye drops, solution.

A clear, transparent solution.

4. Clinical particulars

4.1 Therapeutic indications

ONATOB-DEX is indicated for the prevention and treatment of inflammation, and the prevention of infection, associated with cataract surgery in adults and children aged 2 years and older.

4.2 Posology and method of administration

Posology

Adults, the elderly and children aged 2 years and over: instil one drop into the conjunctival sac of the affected eye(s) four times daily, beginning the day after surgery and continuing throughout the first 24 days of the postoperative period. The dose may be increased to one drop every two hours during the first two days of treatment if needed. Treatment should not be stopped prematurely, and the duration of therapy should be assessed by the ophthalmologist; the dose should be tapered before stopping. Prolonged use should be avoided (see section 4.4).

Paediatric population

Safety and efficacy in children below 2 years of age have not been established.

Method of administration

For ocular use only. To avoid contamination, the dropper tip should not touch the eye or any surface. Nasolacrimal occlusion or gentle eyelid closure after instillation may reduce systemic absorption. If more than one topical ophthalmic product is used, the medicines should be

administered at least 5 minutes apart. Contact lenses should not be worn during treatment of an ocular infection or inflammation.

4.3 Contraindications

- Hypersensitivity to the active substances, to other aminoglycosides or corticosteroids, or to any of the excipients listed in section 6.1.
- Epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella and other viral diseases of the cornea and conjunctiva.
- Mycobacterial ocular infection and fungal diseases of ocular structures.
- Acute untreated purulent ocular infection which may be masked or enhanced by the corticosteroid.

4.4 Special warnings and precautions for use

For topical ophthalmic use only; not for injection into the eye. As with other antibacterials, prolonged use may lead to overgrowth of non-susceptible organisms, including fungi; if superinfection occurs, appropriate therapy should be started. Cross-sensitivity to other aminoglycosides may occur, and hypersensitivity to topical tobramycin may develop.

Corticosteroid-related effects

Prolonged use of topical ophthalmic corticosteroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve and defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation; intra-ocular pressure should be monitored, particularly in children and where treatment continues beyond 10 days. Corticosteroids may reduce resistance to, and aid in the establishment of, secondary ocular infections, and may mask or enhance existing infection. In diseases causing thinning of the cornea or sclera, perforation has been known to occur. The initial prescription and renewal beyond 24 days should be under the supervision of an ophthalmologist. Visual disturbance may be reported with systemic and topical corticosteroid use; if a patient presents with blurred vision or other visual disturbance, referral to an ophthalmologist for evaluation of possible causes (including cataract, glaucoma or rare conditions such as central serous chorioretinopathy) should be considered.

Benzalkonium chloride

If the product contains benzalkonium chloride, this may cause eye irritation and is known to discolour soft contact lenses; contact with soft contact lenses should be avoided.

4.5 Interaction with other medicinal products and other forms of interaction

No specific interaction studies have been performed. Concurrent use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems. Given the low systemic exposure following topical ocular administration, clinically relevant systemic interactions are unlikely; however, caution is advised in patients receiving systemic aminoglycosides, as concurrent use could theoretically add to systemic aminoglycoside exposure.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data on the use of tobramycin/dexamethasone eye drops in pregnant women. Prolonged or repeated corticosteroid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation, and aminoglycosides cross the placenta. ONATOB-DEX should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus, at the lowest effective dose for the shortest time.

Breast-feeding

Systemically administered corticosteroids and aminoglycosides are excreted in breast milk; it is unlikely that topical ocular administration would produce detectable quantities in milk. Caution should nevertheless be exercised.

4.7 Effects on ability to drive and use machines

As with other eye drops, transient blurred vision on instillation may affect the ability to drive or use machines; the patient should wait until vision clears before driving or using machines.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Immune system disorders	Not known	Hypersensitivity
Endocrine disorders	Not known	Adrenal suppression following prolonged intensive use
Nervous system disorders	Uncommon	Dysgeusia, headache
Eye disorders	Common	Increased intra-ocular pressure, ocular discomfort, eye irritation, eye pain, eye pruritus
	Uncommon	Keratitis, ocular hyperaemia, blurred vision, dry eye, eyelid oedema, foreign-body sensation, increased lacrimation
	Not known	Glaucoma with optic-nerve damage, posterior subcapsular cataract, corneal thinning, secondary ocular infection, delayed corneal wound healing, mydriasis, ptosis
Skin and subcutaneous tissue disorders	Uncommon	Eyelid pruritus, eyelid erythema
	Not known	Rash, dermatitis, hypersensitivity of the skin surrounding the eye (an effect associated with topical aminoglycosides)

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 to the National Regulatory Authority.

4.9 Overdose

A topical overdose may be flushed from the eye(s) with lukewarm water. The characteristics of the product make toxic effects unlikely with an ocular overdose or with accidental ingestion of the contents of one bottle. In the event of accidental ingestion, treatment is symptomatic and supportive.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, anti-inflammatory agents and anti-infectives in combination, corticosteroids and anti-infectives in combination. ATC code: S01CA01.

Dexamethasone is a potent corticosteroid that suppresses the inflammatory response to mechanical, chemical or immunological stimuli, inhibiting oedema, capillary dilatation, leucocyte migration and fibroblast proliferation. Tobramycin is an aminoglycoside antibiotic active against a wide range of Gram-negative and some Gram-positive organisms; it inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit. The combination provides an anti-inflammatory corticosteroid together with antibacterial cover to prevent or treat infection in inflammatory ocular conditions where infection or a risk of infection exists, such as following cataract surgery.

5.2 Pharmacokinetic properties

Following topical ocular administration, dexamethasone and tobramycin penetrate the ocular tissues, while systemic absorption is low. Any absorbed dexamethasone is metabolised in the liver and excreted in the urine; absorbed tobramycin is eliminated largely unchanged by renal excretion.

5.3 Preclinical safety data

Dexamethasone and tobramycin are well-established active substances. Non-clinical data reveal no special hazard for humans at clinically relevant topical exposures beyond that reflected in other sections of this Summary of Product Characteristics; systemic aminoglycoside administration in animals is associated with nephrotoxicity and ototoxicity at high exposures.

6. Pharmaceutical particulars

6.1 List of excipients

The full quantitative list of excipients should be confirmed from the applicant's finished-product formulation (3.2.P.1); for a solution of this type it typically includes benzalkonium chloride (preservative), disodium edetate, sodium chloride, tyloxapol or a similar surfactant, sodium sulfate, sodium hydroxide and/or sulfuric acid for pH adjustment, and purified water. Benzalkonium chloride, if present, is an excipient of known effect and must be declared in section 2 and warned in section 4.4.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

To be confirmed from the applicant's stability data. After first opening, the contents should be used within 28 days.

6.4 Special precautions for storage

Store below 25°C. Do not freeze. Protect from light. Keep the bottle tightly closed and out of the reach and sight of children.

6.5 Nature and contents of container

5 mL LDPE dropper bottle with a nozzle and a white cap, presented in a carton together with the leaflet.

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 Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Dawa Limited.

Manufacturer

Theta Pharmaceuticals Limited, F44, 1st Floor, Shagun Arcade CHS, A.K. Vaidya Marg, Opp. HDFC Bank, Malad East, Mumbai City, Maharashtra, India.

8. Marketing Authorisation Number

H2025/CTD11918/25984

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text