

## NEW ZEALAND DATA SHEET

### 1. PRODUCT NAME

Maxitrol™ sterile ophthalmic suspension and ointment.

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of Maxitrol Ophthalmic Suspension contains dexamethasone 1 mg, neomycin sulfate 3,500 IU, polymixin B sulfate 6,000 IU.

Each g of Maxitrol Ophthalmic Ointment contains Dexamethasone 1 mg, neomycin sulfate 3,500 IU, polymixin B sulfate 6,000 IU.

#### Excipient with known effect

Eye Drops: Benzalkonium chloride 0.004% as a preservative.

Eye Ointment: Methyl hydroxybenzoate 0.05% as a preservative.

Propyl hydroxybenzoate 0.01% as a preservative.

For the full list of excipients, see Section 6.1.

### 3. PHARMACEUTICAL FORM

Eye drops, suspension.

Eye ointment.

### 4. CLINICAL PARTICULARS

#### 4.1. Therapeutic indications

Maxitrol is indicated in ocular inflammation when concurrent use of an antimicrobial is judged necessary.

#### 4.2. Dose and method of administration

Keep out of reach of children.

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.

#### Maxitrol Eye Drops

One to two drops topically in the conjunctival sac(s). In severe disease, drops may be used hourly, being tapered to discontinuation as the inflammation subsides. In mild disease, drops may be used up to four to six times daily.

Shake the bottle well before use. Remove the loose collar from the cap when the bottle is first opened. After cap is removed, if tamper evident snap collar is loose, remove before using product.

In order to prevent contamination of the dropper tip and the suspension, caution should be exercised to ensure that the dropper tip does not touch the eyelids, the surroundings of the eye, or any other surfaces.

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.

## Maxitrol Eye Ointment

Apply a small amount into the conjunctival sac(s) up to three or four times daily or, may be used adjunctively with drops at bedtime. Do not let the tip of the tube touch the eye.

### **4.3. Contraindications**

Epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, and many other viral diseases of the cornea and conjunctiva (except herpes zoster keratitis). Mycobacterial infection of the eye. Fungal diseases of ocular structures or untreated parasitic eye infections. Hypersensitivity to dexamethasone, neomycin sulfate, polymixin B sulfate or any other component of the medication. See Section 6.1. for a list of excipients.

Hypersensitivity to the antibiotic component occurs at a higher rate than for other components.

The use of these combinations is always contraindicated after uncomplicated removal of a corneal foreign body.

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

For topical use only. Not for injection.

Prolonged use may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, defects in the visual acuity and fields of vision, and posterior subcapsular cataract formation.

Prolonged use may suppress the host response and thus increase the hazard of secondary bacterial, fungal, parasitic or viral ocular infections and mask the clinical signs of infection. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

If these products are used for 10 days or longer, intraocular pressure should be routinely monitored even though it may be difficult in children and uncooperative patients. 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. Maxitrol is not approved for use in paediatric patients.

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.

Employment of steroid medication in the treatment of herpes simplex requires great caution.

Sensitivity to topically administered aminoglycosides, such as neomycin, may occur in some patients. Severity of hypersensitivity reactions may vary from local effects to generalized reactions such as erythema, itching, urticarial, skin rash, anaphylaxis, anaphylactoid reactions, or bullous reactions. If hypersensitivity develops during use of this medicine, treatment should be discontinued.

Products containing neomycin sulfate may cause cutaneous sensitization.

Cross-hypersensitivity to other aminoglycosides can occur, and the possibility that patients

who become sensitized to topical neomycin may also be sensitive to other topical and/or systemic aminoglycosides should be considered.

Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic neomycin or when applied topically to open wounds or damaged skin. Nephrotoxic and neurotoxic reactions have also occurred with systemic polymyxin B. Although these effects have not been reported following topical ocular use of this product, caution is advised when used concomitantly with systemic aminoglycoside or polymyxin B therapy.

The initial prescription and renewal of the medication order beyond 20 mL or 8 g should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

The possibility of persistent fungal infections of the cornea should be considered after prolonged steroid dosing. If fungal infection occurs, corticosteroids therapy should be discontinued.

As with other anti-infectives, prolonged use of antibiotics such as neomycin and polymyxin may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy.

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 steroids.

Maxitrol ointment contains methyl hydroxybenzoate and propyl hydroxybenzoate which may cause allergic reactions (possibly delayed). It also contains wool fat which may cause local skin reactions (e.g. contact dermatitis).

#### Paediatric use

Safety and effectiveness in paediatric patients have not been established.

#### Hepatic and renal impairment

Maxitrol has not been studied in these subject populations.

#### Contact Lenses

Contact lens wear is not recommended during treatment of an ocular inflammation or infection. Additionally, Maxitrol Eye drops suspension 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 Maxitrol Eye drops suspension and wait at least 15 minutes before reinsertion.

### **4.5 Interactions with other medicinal 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 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.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

There are no adequate or well-controlled studies in pregnant women. Aminoglycoside antibiotics, such as neomycin, do cross the placenta after intravenous dosing in pregnant women. Non-clinical and clinical systemic exposure to aminoglycosides has been shown to induce ototoxicity and nephrotoxicity. Prolonged or repeated corticoid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation.

Studies in animals have shown reproductive toxicity. Maxitrol should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

##### Breast-feeding

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, use only when considered essential by the physician

##### Fertility

There are no available data on the use of this medicine affecting male or female fertility.

#### **4.7 Effects on ability to drive or use machines**

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient must wait until the vision clears before driving or using machinery.

#### **4.8 Undesirable effects**

Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination. Exact incidence figures are not available since no denominator of treated patients is available.

Reactions occurring most often from the presence of the anti-infective ingredient are allergic sensitizations. The reactions due to the steroid components in decreasing order of frequency are: elevation of intraocular pressure (IOP) with possible development of glaucoma, and infrequent optic nerve damage, posterior sub-capsular cataract formation and delayed wound healing.

##### Secondary infection

The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroid. The possibility of fungal invasion must be considered in any persistent corneal ulceration where steroid treatment has been used.

Secondary bacterial ocular infection following suppression of host responses also occurs.

## Post Marketing Experience

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 for Maxitrol Eye drops suspension or Ointment.

### *Eye Disorders*

Uncommon ( $\geq 0.1\%$  to  $< 1\%$ ): keratitis, intraocular pressure increased, vision blurred, photophobia, mydriasis, eyelid ptosis, eye pain, eye swelling, eye pruritus, ocular discomfort, foreign body sensation in eyes, eye irritation, ocular hyperaemia, lacrimation increased.

### *Immune Disorders*

Uncommon ( $\geq 0.1\%$  to  $< 1\%$ ): hypersensitivity.

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.

### *Eye Disorders*

Not Known: ulcerative keratitis, vision blurred, photophobia, mydriasis, eyelid ptosis, eye pain, eye swelling, foreign body sensation in eyes, ocular hyperaemia, lacrimation increased.

### *Immune Disorders*

Not Known: hypersensitivity.

### *Nervous System Disorders*

Not Known: headache.

### *Skin and subcutaneous tissue Disorders*

Not Known: Stevens-Johnson syndrome.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting>.

## **4.9 Overdose**

Due to the characteristics of this preparation, intended for topical use, no toxic effects are expected when administered to the eye neither at the recommended doses nor in the event of accidental ingestion of the contents of a bottle. In case of overdose, treatment should be supportive.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: ophthalmologicals; anti-infectives, ATC code: S01CA01.

#### Mechanism of action

Corticoids suppress the inflammatory response to a variety of agents and they probably delay or slow healing. Since corticoids may inhibit the body's defence mechanism against infection, a concomitant antimicrobial drug may be used when this inhibition is considered to be clinically significant in a particular case.

The anti-infective component in the combination is included to provide action against specific organisms susceptible to it. Neomycin sulfate is considered active against the following microorganisms: Staphylococcus aureus, Corynebacterium diptheriae, Streptococcus viridans, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Aerobacter aerogenes, and Haemophilus influenzae.

Polymyxin B sulfate is considered active against the following microorganisms: Pseudomonas aeruginosa, Aerobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Koch-Weeks bacillus.

When a decision to administer both a corticoid and an antimicrobial is made, the administration of such drugs in combination has the advantage of greater patient compliance and convenience, with the added assurance that the appropriate dosage of both drugs is administered, plus assured compatibility of ingredients when both types of drugs are in the same formulation and, particularly, that the correct volume of drug is delivered and retained.

The relative potency of corticosteroids depends on the molecular structure, concentration and release from the vehicle.

#### Pharmacodynamic effects

No information available.

#### Clinical efficacy and safety

No information is available.

### **5.2 Pharmacokinetic properties**

Not known.

### **5.3 Preclinical safety data**

#### Carcinogenicity, mutagenicity

No information is available.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1. List of excipients**

#### Eye drops, suspension

Benzalkonium chloride as a preservative

Hypromellose

Polysorbate 20

Sodium chloride

Hydrochloric acid

Sodium hydroxide

Purified water.

Eye ointment

Methyl hydroxybenzoate as a preservative

Propyl hydroxybenzoate as a preservative

Lanolin

White soft paraffin.

## **6.2 Incompatibilities**

Not known.

## **6.3 Shelf life**

Eye drops, suspension

24 months.

Eye ointment

48 months.

## **6.4 Special precautions for storage**

Eye drops, suspension

Store below 25° C.

Discard container 4 weeks after opening.

Eye Ointment

Store below 25° C.

Do not refrigerate.

Discard container 4 weeks after opening.

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

Eye drops suspension

5 mL Drop-Tainer™ dispenser.

Eye Ointment

3.5 g aluminium tube.

## **6.6 Special precautions for disposal**

No special requirements for disposal.

## **7. MEDICINE SCHEDULE**

Prescription Only Medicine.

## **8. SPONSOR**

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## **9. DATE OF FIRST APPROVAL**

Eye Drops: 1 March 1968.

Eye Ointment: 1 March 1968.

## **10. DATE OF REVISION OF THE TEXT**

26 March 2018.

Summary Table of Changes

Section 4.4	Addition of all CYP3A4 inhibitors (instead of only ritonavir) in possible cause of Cushing's syndrome and/or adrenal suppression.
Section 4.5	More safety information in regards to the interaction of CYP3A4 inhibitors as drug-drug interaction.

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