NOVARTIS

MAXITROL® Ophthalmic Suspension

Polymyxin B sulphate equal to 6000 international units polymyxin B base, neomycin sulphate equal to 3500 international units neomycin base and dexamethasone 1,0 mg per mL

MAXITROL® Ophthalmic Ointment

Polymyxin B sulphate equal to 6000 international units polymyxin B base, neomycin sulphate equal to 3500 international units neomycin base and dexamethasone 1,0 mg per gram

Professional Information

Document status:	Final
Release date:	25 May 2022

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

MAXITROL® Ophthalmic Suspension

MAXITROL® Ophthalmic Ointment

2 QUALITIVE AND QUANTITIVE COMPOSITION

MAXITROL® Ophthalmic Suspension

Each 1,0 mL contains:

Polymyxin B sulphate equal to 6000 international units polymyxin B base, neomycin sulphate equal to 3500 international units neomycin base and dexamethasone 1,0 mg,

Preservative: Benzalkonium chloride 0,004 % (*m/v)*.

MAXITROL® Ophthalmic Ointment

Each 1,0 g contains:

Polymyxin B sulphate equal to 6000 international units polymyxin B base, neomycin sulphate equal to 3500 international units neomycin base and dexamethasone 1,0 mg,

Preservative: Methylparaben 0,05 % (*m/m*) and propylparaben 0,01 % (*m/m*).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

MAXITROL® Ophthalmic Suspension: White to pale yellow, opaque suspension.

MAXITROL® Ophthalmic Ointment: A greasy, translucent to opaque and white to light yellow, homogeneous ointment, free of lumps.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In the management of infectious ocular inflammations produced by organisms which are sensitive to the antibiotics neomycin sulphate and polymyxin B sulphate.

Acute or chronic non-purulent conjunctivitis, blepharoconjunctivitis and keratoconjunctivitis; non-specific superficial keratitis; deep keratitis; acne rosacea keratitis; iridocyclitis; mild acute iritis; recurrent marginal ulceration and corneal ulcer (use with care in those diseases causing thinning of the cornea because of the danger of perforation); non-purulent blepharitis; scleritis; episcleritis; scleroconjunctivitis; herpes zoster ophthalmicus (do not use in herpes simplex) and post-operatively to aid in the prevention of ophthalmic cases of infections.

4.2 Posology and method of administration

Posology

Adults (including the Elderly):

MAXITROL® Ophthalmic Suspension:

- Instil one to two drops topically in the conjunctival sac(s) four to six times daily.
- Dosage may be reduced after three to four days when satisfactory improvement has been obtained.
- Shake bottle well before use.

MAXITROL® Ophthalmic Ointment:

- Apply a small amount of ophthalmic ointment into the conjunctival sac(s) three to four times daily.
- When favourable response is observed dosage may be reduced gradually to once a day application for several days.

Special populations

Hepatic and renal impairment:

MAXITROL has not been studied in these subject populations. However, due to low systemic absorption of the active substances after topical administration of this product, dose adjustment is not necessary.

Method of administration

- For ocular use only. Not for injection or ingestion.

MAXITROL® Ophthalmic Suspension:

- 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® Ophthalmic Ointment:

- Do not touch the top of the tube to any surface as this may contaminate the contents.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients.
- Contraindicated in tubercular, fungal and most viral lesions of the eye (herpes simplex keratitis), vaccinia, varicella, acute purulent conjunctivitis and acute purulent blepharitis or untreated parasitic eye infections.
- Mechanical lacerations and abrasions.
- Mycobacterial ocular infections.
- Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore, MAXITROL should not be used during pregnancy.

4.4 Special warnings and precautions for use

- 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 Interaction with other medicines and other forms of interactions*). In these cases, treatment should not be discontinued abruptly, but progressively tapered.
- The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetes).
- Topical ophthalmic corticosteroids may slow corneal wound healing. Topical NSAIDs (non-steroidal anti-inflammatory drugs) 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 Interaction with other medicines and other forms of interactions*)

- 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.
- Additionally, topical use of neomycin may lead to a skin 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.
- As with all antibacterial preparation prolonged use may lead to overgrowth of non-susceptible bacterial strains or fungi. If superinfection occurs, appropriate therapy should be initiated.
- Patients using ophthalmic preparations containing neomycin sulphate should be advised to consult a physician if ocular pain, redness, swelling, or irritation worsens or persists.
- Prolonged use of 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. 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.
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.
- Corticosteroids may reduce resistance to and aid in the establishment of nonsusceptible bacterial, fungal, parasitic or viral infections and mask the clinical signs of infection or may suppress hypersensitivity reactions to MAXITROL eye drops, suspension. Fungal infection should be suspected in patients with persistent corneal ulceration who have been or are receiving these drugs; corticosteroid therapy should be discontinued if fungal infection occurs.

MAXITROL® Ophthalmic Suspension:

- As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations cannot be excluded, regular ophthalmological examination is required. Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.
- 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 *(see section 4.2 Posology and method of administration).*

MAXITROL® Ophthalmic Ointment:

• This product contains methylparahydroxybenzoate and propylparahydroxybenzoate which may cause allergic reactions (possibly delayed).

• This product also contains lanolin which may cause local skin reactions (e.g. contact dermatitis).

Visual disturbance

- Visual disturbance may be reported with systemic and topical corticosteroid, as contained in MAXITROL 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.
- Contact lens wear is discouraged during treatment of an ocular infection. Therefore, patients should be advised not to wear contact lenses during treatment with MAXITROL eye drops, suspension.
- In patients receiving systemic corticosteroids, new-onset or exacerbation of pre-existing diabetes mellitus may occur. Because of the possibility of reduced glucose tolerance / diabetes mellitus with topical ophthalmic corticosteroids, caution is recommended when administering MAXITROL to patients with a personal or family history of diabetes.

4.5 Interaction with other medicines and other forms of Interaction

- CYP3A4 inhibitors including ritonavir and cobicistat may increase systemic exposure resulting in increased risk of adrenal suppression / Cushing's syndrome *(see section 4.4 Special warnings and precautions for use).* 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.

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

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/ Contraception in males and females

No information available.

Pregnancy

MAXITROL should not be used during pregnancy.

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. At the low dose administered via this topical product, neomycin is not expected to cause ototoxicity or nephrotoxicity from *in utero* exposure. 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 Special warnings and precautions for use)*.

Breastfeeding

Because systemic corticosteroids and aminoglycosides may be distributed into milk, a risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

There are no available data on the use of neomycin or polymyxin B affecting male or female 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

MAXITROL may cause temporarily blurred vision and has no or negligible effect on mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

4.8 Undesirable effects

a. Summary of the safety profile

Corticosteroids delay wound healing, promote development and spread of infection and may mask evidence of its progression until sight is lost. Perforation has been known to occur with the use of topical steroids in those diseases of the eye which cause thinning of the cornea or sclera. Employment of steroid medication in the treatment of stromal herpes simplex requires great caution; frequent slit lamp microscopy is mandatory. Steroid medication may give rise to serious exacerbations of herpes infections of the eye. Prolonged use may result in glaucoma, damage to the optic nerve, defects in visual acuity and fields of vision, posterior sub capsular cataract formation, or may aid in the establishment of secondary ocular infection from the pathogens liberated from ocular tissue.

As fungal infections of the cornea are particularly prone to develop coincidentally with long-term topical steroid applications, fungus invasion must be suspected in any persistent corneal ulceration where a steroid has been used or is in use.

Prolonged use may give rise to the development of iatrogenic glaucoma. Intraocular pressure should be monitored frequently. If the eye has not responded within 48 hours, the patient should be referred to an ophthalmologist because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma.

Prolonged local use of neomycin should be avoided as it may lead to sensitisation. Hypersensitivity reactions, usually of the delayed type have occurred during local treatment with neomycin but may be masked by the dexamethasone.

Tabulated summary 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 < 1/1000), very rare (< 1/10,000) or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in decreasing order of seriousness. The adverse reactions were obtained from clinical trials and post-marketing experience.

Body system	**Undesirable effect**
Immune system disorders	*Not known:* hypersensitivity (systemic or ocular)
Endocrine disorders	*Not known:* Cushing's syndrome, adrenal suppression (*see section 4.4)*
Nervous system disorders	*Not known:* headache

Eye disorders	*Uncommon:* keratitis, intraocular pressure increased, eye pruritus, ocular discomfort, , eye irritation, *Not known:* ulcerative keratitis, corneal thinning, vision blurred *(see also section 4.4)*, photophobia, mydriasis, eyelid ptosis, eye pain, eye swelling, foreign body sensation in eyes, ocular hyperaemia, increased lacrimation
Skin and subcutaneous tissue disorders	*Not known:* Stevens-Johnson syndrome

Description of selected adverse event

Due to the steroid 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 Special warnings and precautions for use).*

Topical ophthalmic steroid use may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects. Also, it may lead to posterior subcapsular cataract formation *(see section 4.4 Special warnings and precautions for use).*

Sensitivity to topically administered aminoglycosides may occur in some patients *(see section 4.4 Special warnings and precautions for use).* Systemic side effects may occur with extensive use.

Corticosteroids may impair glucose tolerance, which can lead to new-onset or exacerbation of diabetes mellitus *(see section 4.4 Special warnings and precautions for use)*.

Reporting of suspected adverse reactions

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 to SAHPRA via the “Report Drug Reaction Process”, found online under SAHPRA’s safety publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (*see section 4.8 Undesirable effects*).

Discontinue use immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.15.3 Combination antibiotics and/or sulphonamides and corticosteroids.

Pharmacotherapeutic group: ophthalmologicals; anti-infectives.

ATC code: S01CA01

Polymyxin B is effective against Gram-negative bacteria and is bactericidal. The following organisms are highly susceptible**:** *Enterobacter, Escherichia, Haemophilus, Klebsiella, Pasteurella, Salmonella, Shigella, Vibrio* and *Pseudomonas*. Development of resistant strains occur infrequently. Neomycin sulphate is a broad-spectrum antibiotic. Gram-negative species that are highly sensitive are *E. coli*, *Enterobacter*, *Aerobacter aerogenes*, *K. pneumoniae*, *Pasteurella*, *Pr. vulgaris*, *Salmonella*, *Shigella*, *H. influenzae*, *N. meningitidis*, *V. cholerae* and *B. pertussis*.

Gram-positive microorganisms that are inhibited include *Bacillus anthracis*, *C. diphtheriae*, *Staph. aureus*, *Strep. faecalis*, *List. monocytogenes* and *M. tuberculosis*. *Borelia* and *Leptospira interrogans* are also suppressed. The sensitivity of *Pseud. aeruginosa* is variable. Neomycin is active against tubercle bacilli, regardless of their susceptibility to streptomycin. Dexamethasone is a 16-methyl substituted hydrocortisone analogue with the highest anti- inflammatory potency and it readily penetrates the cornea.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

MAXITROL® Ophthalmic Suspension:

Polysorbate 20

Sodium chloride

Hydrochloric acid

and/or Sodium hydroxide

Hydroxypropylmethylcellulose

Benzalkonium chloride

Purified water

MAXITROL® Ophthalmic Ointment:

Anhydrous liquid lanolin

Methyl paraben, Propyl paraben

White petrolatum

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened 24 months.

Discard 28 days after first opening.

6.4 Special precautions for storage

Store in a cool place below 25 °C.

Do not refrigerate.

Do not use more than 28 days after opening.

Store in the original package / container.

6.5 Nature and contents of container

MAXITROL® Ophthalmic Suspension:

Low density polyethylene bottle containing 5 mL.

MAXITROL® Ophthalmic Ointment:

Ophthalmic ointment tube containing 3,5 g.

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

No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Novartis South Africa (Pty) Ltd

Magwa Crescent West

Jukskei View

Waterfall City

Johannesburg

South Africa

2090

8 REGISTRATION NUMBER(S)

MAXITROL® Ophthalmic Suspension: H.1145 (Act 101/1965)

MAXITROL® Ophthalmic Ointment: H.1158 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 September 2011

10 DATE OF REVISION OF TEXT

25 May 2022

MAXITROL® Ophthalmic Suspension	**MAXITROL® Ophthalmic Ointment**
Botswana: S2 Reg. No.: B9301175	Botswana: S2 Reg. No.: B9301180
Namibia: NS2 Reg. No.: 14/13.4.1/0555	Namibia: NS2 Reg. No.: 14/15.2/0559
	Zimbabwe: PP Reg. No.: 98/19.2.2/3322