PRODUCT INFORMATION

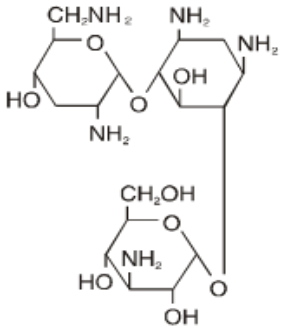
TOBREX* (tobramycin) Eye Drops 0.3%

TOBREX* (tobramycin) Eye Ointment 0.3%

NAME OF THE MEDICINE

Non-proprietary name: Tobramycin Eye Drops 0.3% and Tobramycin Eye Ointment 0.3%

The chemical structure of tobramycin is represented as:



Chemical name: 4-*O*-(3-Amino-3-deoxy-α-D-glucopyranosyl)-2-deoxy-6-*O*-(2,6-diamino-2,3,6-trideoxy-α-D-ribo-hexopyranosyl)-L-streptamine

Empirical formula: $C_{18}H_{37}N_5O_9$

Molecular weight: 467.5

CAS Registry Number: 32986-56-4.

DESCRIPTION

TOBREX (tobramycin) 0.3% Eye Drops and TOBREX (tobramycin) 0.3% Eye Ointment (TOBREX) are sterile topical antibiotic formulations prepared specifically for topical therapy of bacterial eye infections.

Each mL of TOBREX Eye Drops contains:

Active ingredient: tobramycin 0.3% (3 mg).

Preservative ingredient: benzalkonium chloride 0.01% (0.1 mg).

Excipient ingredients: boric acid, sodium sulfate, sodium chloride, tyloxapol, sodium hydroxide and/or sulphuric acid (to adjust pH) and purified water.

TOBREX (tobramycin) Eye Drops has a pH range between 7.0 and 8.0.

Each gram of TOBREX Eye Ointment contains:

Active ingredient: tobramycin 0.3% (3 mg).

Preservative ingredient: chlorobutanol 0.5% (5 mg).

Excipient ingredients: mineral oil and petroleum base.

PHARMACOLOGY

Tobramycin is actively transported across the bacterial cell membrane, and binds to a specific receptor protein on the 30 S subunit of bacterial ribosomes and interferes with an initiation complex between messenger RNA (mRNA) and the 30 S subunit, thus inhibiting protein synthesis.

Microbiology

In vitro data: in vitro studies have demonstrated tobramycin is active against susceptible strains of the following microorganisms:

- *Staphylococci*, including *S. aureus* and *S. epidermidis* (coagulase-positive and coagulase-negative), including penicillin-resistant strains.

- *Streptococci*, including some of the group A - beta-haemolytic species, some non-haemolytic species, and some *Streptococcus pneumoniae*.

- *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis* (indole-negative) and indole-positive *Proteus* species.

Bacterial resistance may develop upon prolonged use.

Tobramycin is not effective against most strains of group D *Streptococci.*

INDICATIONS

TOBREX (tobramycin) Eye Drops and TOBREX (tobramycin) Eye Ointment are topical antibiotics indicated in the treatment of external infections of the eye and its adnexa caused by susceptible bacteria. Appropriate monitoring of bacterial response to topical antibiotic therapy should accompany the use of TOBREX.

CONTRAINDICATIONS

TOBREX (tobramycin) Eye Drops and Eye Ointment are contraindicated in patients with known hypersensitivity to tobramycin or to other aminoglycosides or any other ingredients in this product.

PRECAUTIONS

FOR TOPICAL OPHTHALMIC USE ONLY. NOT FOR INJECTION INTO THE EYE.

Hypersensitivity

Sensitivity to topically administered aminoglycosides 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 with this product, discontinue use and institute appropriate therapy.

If TOBREX (topical tobramycin) Eye Drops or Eye Ointment are administered concomitantly with systemic aminoglycoside antibiotics, care should be taken to monitor the total serum concentration. Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic tobramycin therapy. Although these effects have not been reported following topical ocular use of tobramycin, caution is advised when used concomitantly.

General

As with any antibiotic, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated.

Cross-sensitivity to other aminoglycoside antibiotics may occur. The possibility that patients that become sensitised to topical ocular tobramycin may also be sensitive to other topical and/or systemic aminoglycosides should be considered.

Ophthalmic solutions and ointments may retard corneal wound healing.

Effects on fertility

Studies have not been performed to evaluate the effect of topical ocular administration of TOBREX (tobramycin) Eye Drops or Eye Ointment on human fertility.

Use in Pregnancy

Category B3

There are no adequate, well-controlled studies using the topical administration of TOBREX (tobramycin) Eye Drops or Eye Ointment in pregnant women.

A published retrospective assessment of women receiving parenteral aminoglycosides during pregnancy suggested no detectable teratogenic risk to the foetus. The number of women treated with parenteral tobramycin in this study was very small, 2 in the case group and 4 in the control group and so no firm specific conclusions with regard to tobramycin exposure can be drawn from this study. However, the study concluded that parenteral administration of gentamicin and oral neomycin during pregnancy presents no detectable terotogenic risk to the foetus, when restricted to structural developmental abnormalities. This conclusion can be extended to the class of aminoglycoside antibiotics as a whole.

Studies in animals have shown evidence of an increased occurrence of foetal damage following systemic administration of aminoglycosides to pregnant mothers. There is evidence of selective uptake of aminoglycosides by the foetal kidney resulting in damage (probably reversible) to immature nephrons. Eighth cranial nerve damage has also been reported following in utero exposure to some of the aminoglycosides. Because of their chemical similarity, all aminoglycosides must be considered potentially nephrotoxic and ototoxic to the foetus. It should also be noted that therapeutic blood concentrations in the mother do not equate with safety for the foetus.

There is no firm data concerning the detectable blood concentrations in mothers or tissue concentrations in the foetus. The systemic absorption of tobramycin after topical administration of TOBREX is expected to be low.

TOBREX should be used during pregnancy only if the potential benefit for the mother justifies the potential risk to the foetus otherwise tobramycin is not recommended during pregnancy.

Use in Lactation

There are no adequate, well-controlled studies using the topical administration of TOBREX (tobramycin) Eye Drops or Eye Ointment in women who are breast feeding. It is unknown whether tobramycin is excreted in human milk following topical ocular administration. Tobramycin is excreted in human milk after systemic administration. Risk to the breast fed child cannot be excluded. TOBREX should be used only if the potential benefit for the mother justifies the potential risk to the infant.

Paediatric Use

Safety and effectiveness in children below the age of 1 year have not been established.

Use in the Elderly

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

Renal, Auditory, Vestibular, or Neuromuscular Impairment

Patients receiving concomitant parenteral tobramycin (aminoglycoside) and topical tobramycin therapies should be monitored as clinically appropriate. Caution should be exercised with known or suspected renal, auditory, vestibular, or neuromuscular dysfunction.

Renal and Hepatic Impairment

TOBREX (tobramycin) Eye Drops or Eye Ointment have not been studied in these patient populations. However, due to low systemic absorption of tobramycin after topical administration of this product, dose adjustment is not necessary.

Carcinogenicity and Mutagenicity

No studies have been conducted to evaluate the carcinogenic potential of tobramycin. *In vitro* and *in vivo* studies with tobramycin did not reveal a mutagenic potential

Contact lenses

Neither TOBREX (tobramycin) Eye Drops nor Eye Ointment should be instilled while the patient is wearing contact lenses. Contact lens wear is not recommended during treatment of an ocular infection.

If patients continue to wear contact lenses while under treatment with TOBREX Eye Drops, they should remove their lens(es) prior to instilling the drops in the affected

eye(s). Lens(es) should not be inserted into the eye(s) until 15 minutes after instillation of the drops. TOBREX Eye Drops contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses.

Due to the nature of the ointment base, patients should be advised not to wear their contact lenses while they are being treated with TOBREX Eye Ointment.

Effects on ability to drive and use machines

As with other ophthalmic medications, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs upon application, the patient must wait until the vision clears before driving or using machinery.

INTERACTIONS WITH OTHER MEDICINES

If TOBREX (topical tobramycin) Eye Drops or Eye Ointment are used while the patient is on a systemic aminoglycoside antibiotic, the patient's total serum aminoglycoside concentration should be monitored.

Concurrent and/or sequential use of TOBREX with other drugs with neurotoxic or ototoxic potential should be avoided.

Do not use TOBREX simultaneously with a topical beta lactam type antibiotic as this is likely to result in inactivation of tobramycin.

ADVERSE EFFECTS

The most frequent adverse reactions to TOBREX (tobramycin) Eye Drops and Eye Ointment are localised ocular toxicity and hypersensitivity, including punctate keratitis, eye and lid itching, lid swelling, ocular hyperaemia, conjunctival erythema and lacrimation. These reactions occur in approximately 3% of patients treated with TOBREX.

Other adverse reactions associated with ophthalmic tobramycin are burning and stinging of the eyes. For ophthalmic ointment dosage form: blurred vision.

A summary of treatment emergent adverse events based on literature and postmarketing experience and their estimate of frequencies (very common, common, uncommon, rare, very rare, and not known) in accordance with preferred term and system organ classes (SOC) of any severity are listed below.

Within each frequency-grouping, undesirable effects are presented in decreasing order of seriousness. These adverse reactions were observed following ophthalmic use of Tobramycin Eye Drops and/or Eye Ointment:

Immune system disorders

Uncommon ($> 0.1\%$ to $\leq 1\%$): hypersensitivity.

Not Known: anaphylactic reaction.

Nervous system disorders

Uncommon (> 0.1% to ≤ 1%): headache.

Eye disorders

Common (> 1% to < 10%): ocular discomfort, ocular hyperaemia.

Uncommon (> 0.1% to ≤ 1%): keratitis, corneal abrasion, conjunctival disorder, visual impairment, vision blurred, erythema of eyelid, conjunctival oedema, eyelid oedema, eyelid disorder, eye pain, dry eye, eye discharge, eye pruritus, foreign body sensation in eyes, lacrimation increased.

Not Known: eye allergy, eye irritation, eyelids pruritus.

Skin and subcutaneous tissue disorders

Uncommon (> 0.1% to ≤ 1%): urticaria, dermatitis, madarosis, leukoderma, pruritus, dry skin.

Not Known: Stevens-Johnson syndrome, erythema multiforme, rash.

If topical ocular tobramycin is administered concomitantly with systemic aminoglycoside antibiotics, the possibility of increased systemic toxicity cannot be excluded and care should be taken to monitor the total serum concentration. Prolonged levels above 12 mcg/mL should be avoided.

DOSAGE AND ADMINISTRATION

TOBREX Eye Drops

In mild to moderate disease, instill one or two drops into the affected eye(s) every four hours. In severe infections, instill two drops into the eye(s) hourly until improvement.

TOBREX Eye Ointment

In mild to moderate disease, apply a 1 - 1.5 cm ribbon into the affected eye(s) two or three times per day. In severe infections, apply a 1 - 1.5 cm ribbon every three to four hours until improvement.

Treatment with TOBREX should be reduced prior to discontinuation. The usual duration of treatment is 7-10 days.

OVERDOSAGE

Clinically apparent signs and symptoms of TOBREX (tobramycin) Eye Drops or Eye Ointment overdose are not expected when used as above nor in the event of accidental ingestion of the contents of one bottle or tube. However, excessive local reactions may occur. In such cases treatment should be discontinued and appropriate treatment instituted.

A topical overdose of TOBREX may be flushed from the eye(s) with lukewarm water.

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

POISON SCHEDULE OF THE MEDICINE

Prescription Only Medicine (Schedule 4)

PRESENTATION AND STORAGE CONDITIONS

TOBREX Eye Drops (AUST R 25365)

5 mL DROP-TAINER* dispenser, containing tobramycin 0.3% (3 mg/mL).

TOBREX Eye Ointment (AUST R 25364)

3.5 g ophthalmic tubes containing tobramycin 0.3% (3 mg/g).

Store below 25°C. Discard container 4 weeks after opening.

NAME AND ADDRESS OF SPONSOR

Novartis Pharmaceuticals Australia Pty Limited
ABN 18 004 244 160
54 Waterloo Road
Macquarie Park NSW 2113

DATE OF FIRST INCLUSION IN THE ARTG

12th September 2006

DATE OF MOST RECENT AMENDMENT

26 July 2017

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