SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TOBREX OPHTHALMIC OINTMENT

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g of Tobrex Eye Ointment contains the active ingredient tobramycin 3 mg in 1 g.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye ointment.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Antibiotic for the treatment of eye infections caused by bacteria sensitive to Tobramycin.

4.2. Posology and method of administration

Posology

- In mild disease: a small amount of ointment 2 to 3 times per day,
- In more severe infections: a small amount of ointment every 3 to 4 hours until improvement, following which treatment should be reduced prior to discontinuation.

The length of the treatment is dependent on the origin of the infection and may vary from a couple of days up to some weeks.

Method of administration
For ocular use.

To prevent contamination of the tube tip and ointment, care must be taken not to touch the eyelids, surrounding areas, or other surfaces with the tube tip.
Keep the tube tightly closed when not in use.

In case of concomitant therapy with other topical ocular medicines, an interval of 5 – 10 minutes should be allowed between successive applications.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Hypersensitivity to aminoglycosides.

4.4. Special warnings and precautions for use

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 Eye Ointment is 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 aminoglycosides therapy. Caution is advised when Tobrex Eye Ointment is used concomitantly with systemic aminoglycosides.

Caution should be exercised when prescribing Tobrex Eye Ointment to patients with known or suspected neuromuscular disorders such as myasthenia gravis or Parkinson's disease. Aminoglycosides may aggravate muscle weakness because of their potential effect on neuromuscular function.

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.

Eye ointments may retard corneal wound healing.

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 Eye Ointment has 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.

Contact lenses

Tobrex Eye Ointment should not be instilled while the patient is wearing contact lenses. Contact lens wear is not recommended during treatment of an ocular infection.

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.

4.5 Interactions with other medicinal products and other forms of interactions

If Tobrex Eye Ointment is 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B3.

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

A published retrospective assessment of women receiving parenteral aminoglycosides during pregnancy suggested no detectable teratogenic risk to the fetus. 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 fetus, when restricted to structural developmental abnormalities. This conclusion can be extended to the class of aminoglycoside antibiotics as a whole.

There are no firm data concerning the detectable blood concentrations in mothers or tissue concentrations in the fetus. 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 fetus otherwise tobramycin is not recommended during pregnancy.

Refer to section 5.3 for pre-clinical reproductive studies on aminoglycosides.

Breast-feeding

There are no adequate, well-controlled studies using the topical administration of Tobrex 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.

Fertility

Studies have not been performed to evaluate the effect of topical ocular administration of Tobrex Eye Ointment on human fertility.

4.7 Effects on ability to drive or 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.

4.8 Undesirable effects

The most frequent adverse reactions to Tobrex 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:

Immune system disorders

Uncommon (> 0.1% to ≤ 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 micrograms/mL should be avoided.

Reporting of suspected adverse reactions

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:

https://sideeffects.health.gov.il

4.9 Overdose

Clinically apparent signs and symptoms of Tobrex Eye Ointment overdose are not expected when used as above nor in the event of accidental ingestion of the contents of 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sensory organ; ophthalmologicals; antibiotics

ATC Code: SO1AA12.

Mechanism of action

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.

Pharmacodynamic effects

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.*

5.2 Pharmacokinetic properties

Not available.

5.3 Preclinical safety data

Pregnancy

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 fetus. It should also be noted that therapeutic blood concentrations in the mother do not equate with safety for the fetus.

Carcinogenicity

No studies have been conducted to evaluate the carcinogenic potential of tobramycin.

Mutagenicity

In vitro and in vivo studies with tobramycin did not reveal a mutagenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Mineral Oil (Liquid paraffin)

Chlorobutanol anhydrous

White soft paraffin.

6.2 Incompatibilities

Unknown.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Do not store above 25°C.

Contents should be discarded four weeks after first opening.

6.5 Nature and contents of container

Tobrex Eye Ointment comes in 3.5 g aluminum tube.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MANUFACTURER

ALCON COUVREUR, BELGIUM

RIJKSWEG 14, 2870 PUURS, BELGIUM

.8. LICENSE HOLDER

NOVARTIS ISRAEL LTD

P.O.B 7126, Tel Aviv

9. LICENSE NUMBER(S)

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The content of a prescribing information approved by Ministry of Health in June 2015. Prescribing information was updated according to the guidelines of the ministry of health in April 2020