NOVARTIS

TOBREX® Eye Drops (tobramycin)

3,0 mg/ml, Eye Drops, Solution

TOBREX® Eye Ointment (tobramycin)

3 mg/g, Eye Ointment

Professional Information

Document status: Final

Release date: 05 December 2021

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

TOBREX® eye drops, solution

TOBREX® eye ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TOBREX® eye drops: A sterile ophthalmic solution containing 3 mg tobramycin base per one mL.

Excipient with known effect

preserved with 0,01 % (m/v) benzalkonium chloride.

TOBREX® eye ointment: A sterile ophthalmic ointment containing 3 mg tobramycin base per one gram, preserved with chlorobutanol 0,5 % (m/m).

for full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Eye drops, solution

A colourless to pale yellow or brown solution

Eye ointment

White or off-white homogenous ointment

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TOBREX is a topical antibiotic indicated in the treatment of external bacterial infections of the eye and its adnexa caused by susceptible organisms. Appropriate monitoring of bacterial response to topical antibiotic therapy should accompany the use of TOBREX.

4.2 Posology and method of administration

Posology

TOBREX eye drops, solution:

- For mild to moderate infections, Instil 1 to 2 drops into the conjunctival sac of the affected eye(s) every four hours for seven days.
- In severe infections instil two drops into the conjunctival sac of the affected eye(s) every hour until improvement following which, dosage should be reduced prior to discontinuation.

TOBREX eye ointment:

- In mild to moderate disease, apply a ribbon of about 10 mm (1/2 inch) into the affected eye(s) two or three times per day.
- In severe infections, instil a ribbon of about 10 mm (1/2 inch) into the affected eye(s) every three to four hours until improvement following which treatment should be reduced prior to discontinuation.

4.3 Contraindications

TOBREX is contra-indicated in patients hypersensitive to tobramycin or to any of the excipients.

4.4 Special warnings and precautions for use

- Sensitivity to topically applied aminoglycosides may occur in some patients. If a sensitivity reaction to tobramycin occurs, discontinue use.
- Cross-hypersensitivity to other aminoglycosides can occur, and the possibility that patients who become sensitized to topical ocular tobramycin 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 aminoglycoside therapy. Caution is advised when TOBREX is used concomitantly with systemic aminoglycosides.
- Caution should be exercised when prescribing TOBREX 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.
- Localised ocular toxicity and hypersensitivity can occur. If topical ocular tobramycin is administered concomitantly with systemic aminoglycoside antibiotics, care should be taken to monitor the total serum concentration.
- Prolonged use may lead to skin sensitisation or result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated.
- Ophthalmic ointments may retard corneal healing.

- 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 preparations such as TOBREX 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.
- Contact lens wear is not recommended during treatment of an ocular infection.
- TOBREX Eye Drops contain benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses.
- In case patients are allowed to wear contact lenses, they must be instructed to remove contact lenses prior to application of TOBREX Eye Drops and wait at least 15 minutes before reinsertion.

4.5 Interaction with other medicines and other forms of interactions

No clinically relevant interactions have been described with topical ocular dosing.

Care should be exercised when tobramycin is given to patients receiving other drugs with neuromuscular blocking activity or which are ototoxic. Tobramycin and carbenicillin have been reported to have an enhanced effect. However, since an in vitro incompatibility with carbenicillin sodium has been demonstrated, the two antibiotics should be administered separately when both are required.

4.6 Fertility, pregnancy and lactation

Fertility

Not applicable

Pregnancy

There are no adequate and well controlled studies of tobramycin in pregnant women.

Therefore, this drug should only be used during pregnancy if the potential benefits outweigh the possible risks

Breastfeeding

Because of the potential for adverse reactions in nursing infants from TOBREX, a decision should be made whether to discontinue nursing the infant or discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The following adverse reactions have been reported during clinical trials with TOBREX and are classified according to the subsequent convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	**Adverse reactions**
Immune system disorders	*Uncommon:* hypersensitivity

Nervous system disorders	*Uncommon:* headache
Eye disorders	*Common:* ocular discomfort, ocular hyperaemia *Uncommon:* keratitis, corneal abrasion, visual impairment, vision blurred, erythema of eyelid, conjunctival oedema, eyelid oedema, eye pain, dry eye, eye discharge, eye pruritus, lacrimation increased.
Skin and Subcutaneous Tissue Disorders	*Uncommon:* urticaria, dermatitis, madarosis, leukoderma, pruritus, dry skin

Additional adverse reactions identified from post-marketing surveillance include the following. Frequencies cannot be estimated from the available data.

System Organ Classification	**Adverse reactions**
Immune system disorders	Anaphylactic reaction
Eye disorder	Eye allergy, eye irritation, eyelids pruritus
Skin and subcutaneous tissue disorders	Rash

4.9 Overdose

Due to the characteristics of this preparation, no toxic effects are to be expected with an ocular overdose of this product, or in the event of accidental ingestion of the contents of one bottle or tube.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ophthalmologicals; anti-infectives; antibiotic

ATC code: S01AA12 tobramycin

Pharmacodynamic effects

Tobramycin is a basic water-soluble aminoglycoside antibiotic with a spectrum of activity similar to that of gentamicin. It is active *in vitro* against *Staph. aureus*, most of the family Enterobacteriaceae, and *Pseud. aeruginosa*. Most staphylococci are inhibited by 1 ug/ml or less; most gram-negative bacteria by 2 ug/ml or less, and Pseudomonas, by 5 to 10 ug/ml or less. About 70 % of Klebsiella and Enterobacter (aerobacter) are suppressed by 0,75 ug/ml and over 50 % of *E. Coli* and indole-positive and -negative Proteus are inhibited by at least 3 ug/ml. Tobramycin is bactericidal for susceptible microbial species. It is less active *in vitro* than gentamicin for most gram-negative bacteria but at least two to four times more active against Pseudomonas. There is evidence of transmissible resistance, although some organisms, especially staphylococci, may be resistant to other aminoglycosides and sensitive to tobramycin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

TOBREX® eye drops

Benzalkonium chloride

Boric acid

Tyloxapol

Sodium chloride

Sodium sulphate anhydrous

Sulphuric acid (to adjust pH)

Sodium hydroxide (to adjust pH)

Purified water

TOBREX® eye ointment

Chlorobutanol

Liquid paraffin

White soft paraffin

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

TOBREX® eye drops: 36 months

Do not use more than 30 days after opening

TOBREX® eye ointment: 36 months

Do not use more than 30 days after opening

6.4 Special precautions for storage

TOBREX® eye drops:

Store at or below 25 ºC.

TOBREX® eye Ointment:

Store below at or 25 ºC

6.5 Nature and contents of container

TOBREX® eye drops: Low density polyethylene ophthalmic plastic bottle with a plastic dispensing plug and a plastic closure, containing 5 ml.

TOBREX® eye Ointment: Ophthalmic ointment tube containing 3,5 g.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novartis South Africa (Pty) Ltd

Magwa Crescent West

Waterfall City, Jukskei View

Johannesburg

2090

8. REGISTRATION NUMBER(S)

TOBREX® eye drops: P/15.1/58

TOBREX® eye ointment: P/15.1/205

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

TOBREX® Eye Drops: 30 September 2011

TOBREX® Eye Ointment: 30 September 2011

10. DATE OF REVISION OF TEXT

05 December 2021

TOBREX® eye drops	**TOBREX® eye ointment**
Botswana: S2	Botswana: S2
Reg. No.: B9301215	Reg. No.: B9301220

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