## 1. NAME OF THE MEDICINAL PRODUCT

**TOBRADEX®** 0.3% + 0.1% sterile ophthalmic suspension
(tobramycin and dexamethasone)

**TOBRADEX®** 0.3% + 0.1% sterile ophthalmic ointment
(tobramycin and dexamethasone)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

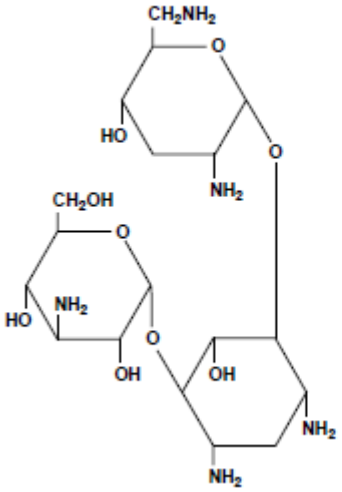
**TOBRADEX ophthalmic suspension**
1 mL of suspension contains 3 mg tobramycin and 1 mg dexamethasone.
Preservative: 1 mL of suspension contains 0.1 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

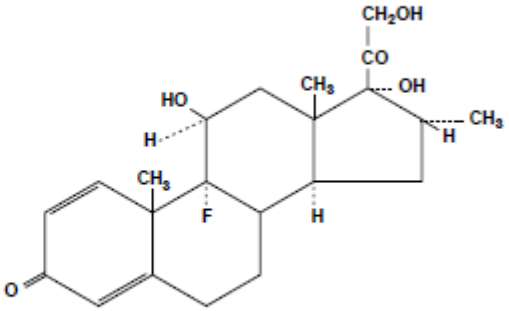
**TOBRADEX ophthalmic ointment**
1 g of ointment contains 3 mg tobramycin and 1 mg dexamethasone.
Preservative: 1 g of ointment contains 5 mg chlorobutanol.

For the full list of excipients, see section 6.1.

The chemical structures for tobramycin and dexamethasone are presented below:




Tobramycin
Empirical formula: $C_{18}H_{37}N_5O_9$
Chemical Name:
*O*-3-Amino-3-deoxy-α-D-glucopyranosyl-(1→4)-*O*-(2,6-diamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranosyl-(1→6)-2-deoxy-L-streptamine




Dexamethasone
Empirical formula: $C_{22}H_{29}FO_5$
Chemical name:
9-Fluoro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione

## 3. PHARMACEUTICAL FORM

**TOBRADEX ophthalmic suspension**
Sterile ophthalmic suspension.
White to off-white suspension.

**TOBRADEX ophthalmic ointment**
Sterile ophthalmic ointment.
White to off-white homogeneous ointment.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

TOBRADEX contains tobramycin, an antibiotic, and dexamethasone, a corticosteroid.

TOBRADEX is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.
Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in oedema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns or penetration of foreign bodies.
The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.
The particular anti-infective drug in this product is active against the common bacterial eye pathogens listed in section 5.1.

### 4.2 Posology and method of administration

**Tobradex ophthalmic suspension**
Posology
1 or 2 drops instilled into the conjunctival sac(s) every 4 to 6 hours. During the initial 24 to 48 hours, the dosage may be increased to 1 or 2 drops every 2 hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

*Use in children*
The safety and efficacy of TOBRADEX ophthalmic suspension in children have not been established.

*Use in patients with hepatic or renal impairment*
The safety and efficacy of TOBRADEX ophthalmic suspension in patients with hepatic or renal impairment have not been established. However, due to low systemic absorption of tobramycin and dexamethasone after topical administration of this product, dose adjustment is not necessary.

Method of administration
For ocular use.

Shake well before use.

After cap is removed, if tamper evident snap collar is loose, remove before using product.

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

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.

If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last.

**Tobradex ophthalmic ointment**
Posology
Apply a small amount, approximately 1/2 inch (1 - 1.5 cm) ointment ribbon, into the conjunctival sac(s) up to 3 or 4 times daily.

TOBRADEX ophthalmic ointment may be used at bedtime in conjunction with TOBRADEX ophthalmic suspension used during the day. Not more than 20 mL or 8 g should be prescribed initially and the prescription should not be refilled without further evaluation as outlined in section 4.4.

*Use in children*
The safety and efficacy of TOBRADEX ophthalmic ointment in children have not been established.

*Use in patients with hepatic or renal impairment*
The safety and efficacy of TOBRADEX ophthalmic ointment in patients with hepatic or renal impairment have not been established. However, due to low systemic absorption of tobramycin and dexamethasone after topical administration of this product, dose adjustment is not necessary.

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.

If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last.

## 4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Herpes simplex keratitis.
- Vaccinia, varicella and other viral infection of cornea or conjunctiva.
- Fungal diseases of ocular structures or untreated parasitic eye infections.
- Mycobacterial ocular infections.
- The use of TOBRADEX is always contraindicated after uncomplicated removal of a foreign body.

## 4.4 Special warnings and precautions for use

- Not for injection into the eye.
- 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, urticaria, skin rash, anaphylaxis, anaphylactoid reactions or bullous reactions. If hypersensitivity develops during use of this medicine, treatment should be discontinued.
- Cross-hypersensitivity to other aminoglycosides can occur, and the possibility that patients who become sensitized to topical 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 TOBRADEX is used concomitantly with systemic aminoglycosides and care should be taken to monitor the total serum concentration.
- Caution should be exercised when prescribing TOBRADEX 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.
- Prolonged use of topical 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 (IOP) 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. TOBRADEX 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). (See section 4.5). In these cases, treatment should not be discontinued abruptly, but progressively tapered.
- Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral, fungal or parasitic infections and mask the clinical signs of infection.
- Fungal infection should be suspected in patients with persistent corneal ulceration. If fungal infection occurs, corticosteroids therapy should be discontinued.
- Prolonged use of antibiotics such as tobramycin may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated.

- Topical ophthalmic corticosteroids may slow corneal wound healing. Topical non-steroidal anti-inflammatory drugs (NSAIDs) 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).
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.
- Contact lens wear is not recommended during treatment of an ocular inflammation or infection. TOBRADEX ophthalmic suspension contains 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 TOBRADEX ophthalmic suspension and wait at least 15 minutes before reinsertion.
- When multiple prescriptions are required, or whenever clinical judgement dictates, the patient should be examined with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

## 4.5 Interaction with other medicinal products and other forms of interaction

- 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 or limited amount of data from the topical ocular use of tobramycin or dexamethasone in pregnant women. Tobramycin does cross the placenta into the foetus after intravenous dosing in pregnant women. Tobramycin is not expected to cause ototoxicity 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.
Studies in animals have shown reproductive toxicity after systemic administration of tobramycin and dexamethasone. These effects were observed at exposures considered sufficiently in excess of the maximum human ocular dosage delivered from the maternal use of the product. Tobramycin has not been shown to induce teratogenicity in rats or rabbits. The ocular administration of 0.1% dexamethasone resulted in foetal anomalies in rabbits (see section 5.3).

TOBRADEX is not recommendend during pregnancy.

**Lactation**
Tobramycin is excreted in human milk after systemic administration. No data is available on the passage of dexamethasone into human breast milk. It is unknown whether tobramycin or dexamethasone are excreted in human milk following topical ocular administration. It is not likely that the amount of tobramycin and dexamethasone would be detectable in human milk or be capable of producing clinical effects in the infant following topical use of the product. A risk to the suckling child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue or abstain from therapy with TOBRADEX taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

**Fertility**
Studies have not been performed to evaluate the effect of tobramycin and dexamethasone on human or animal fertility. There is limited clinical data to evaluate the effect of dexamethasone on male or female fertility. Dexamethasone was free of adverse effects on fertility in a chorionic gonadotropin primed rat model.

## 4.7 Effects on ability to drive and use machines

TOBRADEX has no or negligible influence on the ability to drive and use machines.

However, 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

**Tabulated summary of adverse reactions**
The following adverse reactions have been identified during clinical trials and post-marketing surveillance. They 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 <1/1,000), very rare (<1/10,000) or not known (cannot be estimated from the available data; data from post-marketing surveillance). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

| System organ class | Adverse reactions |
|---|---|
| Immune system disorders | *Not known:* anaphylactic reaction, hypersensitivity |
| Nervous system disorders | *Not known:* dizziness, headache |
| Eye disorders | *Uncommon:* intraocular pressure increased, eye pain, eye pruritus, ocular discomfort, eye irritation<br>*Rare:* keratitis, eye allergy, vision blurred, dry eye, ocular hyperaemia<br>*Not known:* eyelid oedema, erythema of eyelid, mydriasis, lacrimation increased |
| Gastrointestinal disorders | *Rare:* dysgeusia<br>*Not known:* nausea, abdominal discomfort |
| Skin and subcutaneous tissue disorders | *Not known:* erythema multiforme, rash, swelling face, pruritus |

**Description of selected adverse reactions**
- Prolonged use of topical ophthalmic corticosteroids may result in increased intraocular pressure with possible development of glaucoma and damage to the optic nerve, reduced visual acuity and visual field defects, posterior subcapsular cataract formation and delayed wound healing (see section 4.4).
- Due to the corticosteroid 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).
- The development of secondary infection has occurred after the use of combinations containing corticosteroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long term applications of steroids (see section 4.4).
- Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic tobramycin therapy (see section 4.4).
- Sensitivity to topically administered aminoglycosides may occur in some patients (see section 4.4). The most frequent adverse reactions to topical ocular tobramycin (TOBREX®) are localized ocular toxicity and hypersensitivity, including lid itching and swelling, and conjunctival erythema. These reactions occur in less than 4% of patients.

### 4.9 Overdose

An ocular overdose of TOBRADEX may be flushed from the eye(s) with lukewarm water.

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.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-inflammatory agents and anti-infectives in combination – corticosteroids and anti-infectives in combination. ATC code: S01CA01.

**Mode of Action**
<u>Dexamethasone</u>
Topical corticosteroids exert an anti-inflammatory action and have been used for the treatment of anterior inflammation since the 1950s. Aspects of the inflammatory process such as oedema, fibrin deposition,

capillary dilation, leukocyte migration, capillary proliferation, deposition of collagen, scar formation and fibroblastic proliferation are suppressed. Topical corticosteroids are effective in acute inflammatory conditions of the conjunctiva, sclera, cornea, lids, iris and anterior segment of the globe as well as in ocular allergic conditions.

Dexamethasone is one of the most potent corticosteroids; it is 5 to 14 times more potent than prednisolone and 25 to75 times more potent than cortisone and hydrocortisone. Of paramount importance with regard to local therapy is the fact that dexamethasone is over 2000 times more soluble than hydrocortisone or prednisolone. The exact mechanism of anti-inflammatory action of dexamethasone is unknown. It inhibits multiple inflammatory cytokines and produces multiple glucocorticoid and mineralocorticoid effects.

Dexamethasone is a potent corticoid. Corticoids suppress the inflammatory response to a variety of agents and they can 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 clinically significant. Tobramycin is an antibacterial drug. It inhibits the growth of bacteria by inhibiting protein synthesis.

Tobramycin
The preparation contains tobramycin, a rapidly bactericidal aminoglycoside antibiotic. It exerts its primary effect on bacterial cells by inhibiting polypeptide assembly and synthesis on the ribosome.

**Mechanism of resistance**
Resistance to tobramycin occurs by several different mechanisms including (1) alterations of the ribosomal subunit within the bacterial cell, (2) interference with the transport of tobramycin into the cell and (3) inactivation of tobramycin by an array of adenylylating, phosphorylating and acetylating enzymes. Genetic information for production of inactivating enzymes may be carried on the bacterial chromosome or on plasmids. Cross resistance to other aminoglycosides may occur.

**Breakpoints**
The breakpoints and the *in vitro* spectrum as mentioned below are based on systemic use. These breakpoints might not be applicable on topical ocular use of the medicinal product as higher concentrations are obtained locally and the local physical/chemical circumstances can influence the activity of the product on the site of administration. In accordance with EUCAST, the following breakpoints are defined for tobramycin:

- *Enterobacteriaceae* S ≤ 2 mg/L, R > 4 mg/L
- *Pseudomonas spp.* S ≤ 4 mg/L, R > 4 mg/L
- *Acinetobacter spp.* S ≤ 4 mg/L, R > 4 mg/L
- *Staphylococcus spp.* S ≤ 1 mg/L, R > 1 mg/L
- Not species-related S ≤ 2 mg/L, R > 4 mg/L

**Clinical efficacy against specific pathogens**
The information listed below gives only an approximate guidance on probabilities whether microorganisms will be susceptible to tobramycin in TOBRADEX. Bacterial species that have been recovered from external infections of the eye such as observed in conjunctivitis are presented here.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of tobramycin in at least some types of infections is questionable.

| COMMONLY SUSCEPTIBLE SPECIES |
|---|
| Aerobic Gram-positive microorganisms: |
| *Bacillus megaterium*<br>*Bacillus pumilus*<br>*Corynebacterium macginleyi*<br>*Corynebacterium pseudodiphtheriticum*<br>*Kocuria kristinae*<br>*Staphylococcus aureus* (methicillin susceptible – MSSA) |

*Staphylococcus epidermidis* (coagulase-positive and –negative)
*Staphylococcus haemolyticus* (methicillin susceptible – MSSH)
*Streptococci* (including some of the group A beta-hemolytic species, some non-hemolytic species and some *Streptococcus pneumoniae*)

Aerobic Gram-negative microorganisms:

*Acinetobacter calcoaceticus*
*Acinetobacter junii*
*Acinetobacter ursingii*
*Citrobacter koseri*
*Enterobacter aerogenes*
*Escherichia coli*
*H. aegyptius*
*Haemophilus influenzae*
*Klebsiella oxytoca*
*Klebsiella pneumoniae*
*Morganella morganii*
*Moraxella catarrhalis*
*Moraxella lacunata*
*Moraxella oslonensis*
Some *Neisseria* species
*Proteus mirabilis*
Most *Proteus vulgaris* strains
*Pseudomonas aeruginosa*
*Serratia liquifaciens*

Anti-bacterial activity against other relevant pathogens

SPECIES FOR WHICH ACQUIRED RESISTANCE MIGHT BE A PROBLEM

*Acinetobacter baumanii*
*Bacillus cereus*
*Bacillus thuringiensis*
*Kocuria rhizophila*
*Staphylococcus aureus* (methicillin resistant – MRSA)
*Staphylococcus haemolyticus* (methicillin resistant – MRSH)
*Staphylococcus*, other coagulase-negative spp.
*Serratia marcescens*

INHERENTLY RESISTANT ORGANISMS

Aerobic Gram-positive microorganisms:

*Enterococcus faecalis*
*Streptococcus mitis*
*Streptococcus pneumoniae*
*Streptococcus sanguis*
*Chryseobacterium indologenes*

Aerobic Gram-negative microorganisms:

*Haemophilus influenzae*
*Stenotrophomonas maltophilia*

Anaerobic bacteria:

*Propionibacterium acnes*

Bacterial susceptibility studies demonstrate that in some cases, microorganisms resistant to gentamicin retain susceptibility to tobramycin.

**PK/PD relationship**
A specific PK/PD relationship has not been established for TOBRADEX. Dexamethasone has demonstrated dose-independent pharmacokinetics in published animal studies.

Published *in vitro* and *in vivo* studies have shown that tobramycin features a prolonged post-antibiotic effect, which effectively suppresses bacterial growth despite low serum concentrations. Systemic administration studies of tobramycin have reported higher maximum concentrations with once daily compared to multiple daily dosing regimens. However, the weight of current evidence suggests that once daily systemic dosing is equally as efficacious as multiple daily dosing. Tobramycin exhibits a concentration-dependent antimicrobial kill and greater efficacy with increasing levels of antibiotic above the minimum inhibitory concentration (MIC) or minimum bactericidal concentration (MBC).

**Data from clinical studies**
Cumulative safety data from pharmacodynamics clinical studies are presented in section 4.8.

**Geriatric patients**
No overall clinical differences in safety or efficacy have been observed between the elderly and other adult populations.

## 5.2 Pharmacokinetic properties

**Absorption**
Tobramycin is poorly absorbed across the cornea and conjunctiva when administered by topical ocular route. A peak concentration of 3 micrograms/mL in aqueous humour after 2 hours was attained followed by a rapid decline after topical administration of 0.3% tobramycin.

However, TOBRADEX delivers 542 ± 425 micrograms/mL tobramycin in human tears at 2 minutes after ocular dosing, a concentration that generally exceeds the MIC of the most resistant isolates (MICs > 64 micrograms/mL).

Peak dexamethasone concentrations in aqueous humour after administration of TOBRADEX were attained approximately at 2 hours with a mean value 32 ng/mL.

Systemic absorption of tobramycin after TOBRADEX administration was poor with plasma concentrations generally below the limit of quantitation.

Plasma concentrations of dexamethasone were observed but were very low with all values less than 1 ng/mL after TOBRADEX administration.

The bioavailability of oral dexamethasone ranged from 70 to 80% in normal subjects and patients. Tobramycin is not bioavailable orally.

**Distribution**
For tobramycin, systemic volume of distribution is 0.26 L/kg in man. Human plasma protein binding of tobramycin is low at less than 10%.

For dexamethasone, the volume of distribution at steady state was 0.58 L/kg after intravenous administration. The plasma protein binding of dexamethasone is 77%.

**Biotransformation**
Tobramycin is not metabolized while dexamethasone is principally metabolized to 6beta-hydroxydexamethasone along with the minor metabolite 6beta-hydroxy-20-diydrodexamethasone.

**Elimination**
Tobramycin is excreted rapidly and extensively in the urine via glomerular filtration and primarily as unchanged drug. Systemic tobramycin clearance was 1.43 ± 0.34 mL/min/kg for normal weight patients after intravenous administration and its systemic clearance decreased proportionally to renal function. The plasma half-time for tobramycin is approximately 2 hours.

With dexamethasone after intravenous administration, the systemic clearance was 0.125 L/hr/kg with 2.6% of the dose recovered as unchanged parent drug while 70% of the dose was recovered as metabolites.

The half-life has been reported as 3 to 4 hours but was found to be slightly longer in males. This observed difference was not attributed to changes in dexamethasone systemic clearance but to differences in volume of distribution and body weight.

**Linearity/non-linearity**
Ocular or systemic exposure with increasing dosing concentrations of tobramycin after topical ocular administration of tobramycin has not been tested. Therefore, the linearity of exposure with topical ocular dose could not be established. Mean $C_{max}$ for dexamethasone at a topical ocular dose concentration of 0.033% with 0.3% tobramycin appeared lower than with TOBRADEX with a value of approximately 25 ng/mL but this decrease was not proportional to dose.

**Hepatic and renal impairment**
The pharmacokinetics of tobramycin or dexamethasone with TOBRADEX administration has not been studied in these patient populations.

**Effect of age on pharmacokinetics**
There is no change in tobramycin pharmacokinetics in older patients when compared to younger adults. No correlation between age and plasma concentrations of dexamethasone was observed after oral administration of dexamethasone as well.

### 5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans from topical ocular exposure to tobramycin or dexamethasone based on conventional repeated-dose topical ocular toxicity studies, genotoxicity and carcinogenicity studies. Effects in non-clinical reproductive and developmental studies with tobramycin and dexamethasone were observed only at exposures considered sufficiently in excess of the maximum human ocular dosage indicating little relevance to clinical use for low-dose short-term courses of therapy.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

**TOBRADEX ophthalmic suspension**
Benzalkonium chloride, tyloxapol, edetate disodium, sodium chloride, hydroxyethyl cellulose, sodium sulfate, sulfuric acid and/or sodium hydroxide (to adjust pH) and purified water.

**TOBRADEX ophthalmic ointment**
Chlorobutanol, mineral oil and white petrolatum.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Special precautions for storage

**TOBRADEX ophthalmic suspension**
See folding box. Do not freeze.
Do not use this medicine after the expiry date which is stated on the packaging.
Keep this medicine out of the sight and reach of children.

**TOBRADEX ophthalmic ointment**
See folding box. Do not refrigerate.
Do not use this medicine after the expiry date which is stated on the packaging.
Keep this medicine out of the sight and reach of children.

### 6.4 Nature and contents of container

TOBRADEX ophthalmic suspension: DROP-TAINER® dispenser containing 5 mL.
TOBRADEX ophthalmic ointment: tube containing 3.5 g.

Not all presentations may be registered/marketed.

### 6.5 Special precautions for disposal

No special requirements.

**Manufactured by:**

ALCON-COUVREUR
B-2870 Puurs (Belgium) for Novartis Pharma AG, Basel, Switzerland