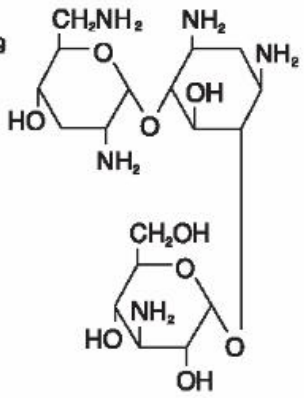
TOBRADEX- tobramycin and dexamethasone ointment
Novartis Pharmaceuticals Corporation

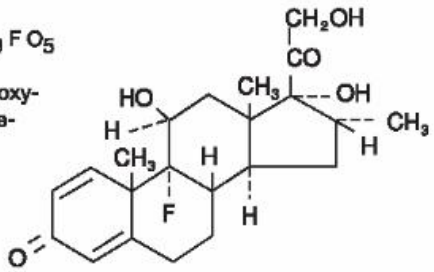
TobraDex® (tobramycin and dexamethasone ophthalmic ointment) Sterile

DESCRIPTION: TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment) is a sterile, multiple dose antibiotic and steroid combination for topical ophthalmic use. 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
MW=467.52



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
MW=392.47



Each gram of TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment) contains: Actives: tobramycin 0.3% (3 mg) and dexamethasone 0.1% (1 mg). **Preservative:** chlorobutanol 0.5%. **Inactives:** mineral oil and white petrolatum.

CLINICAL PHARMACOLOGY: Corticoids suppress the inflammatory response to a variety of agents and they probably delay or slow healing. Since corticoids may inhibit the body's defense mechanism against infection, a concomitant antimicrobial drug may be used when this inhibition is considered to be clinically significant. Dexamethasone is a potent corticoid.

The antibiotic component in the combination (tobramycin) is included to provide action against susceptible organisms. *In vitro* studies have demonstrated that 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-hemolytic species, some nonhemolytic species, and some *Streptococcus pneumoniae*.

Pseudomonas aeruginosa, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Morganella morganii*, most *Proteus vulgaris* strains, *Haemophilus influenzae* and *H. aegyptius*, *Moraxella lacunata*, *Acinetobacter calcoaceticus* and some *Neisseria* species.

No data are available on the extent of systemic absorption from TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment); however, it is known that some

systemic absorption can occur with ocularly applied drugs.

INDICATIONS AND USAGE: TOBRADEX (tobramycin and dexamethasone ophthalmic ointment) 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 edema 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 following common bacterial eye pathogens:

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

Streptococci, including some of the Group A-beta-hemolytic species, some nonhemolytic species, and some *Streptococcus pneumoniae*.

Pseudomonas aeruginosa, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Morganella morganii*, most *Proteus vulgaris* strains, *Haemophilus influenzae* and *H. aegyptius*, *Moraxella lacunata*, *Acinetobacter calcoaceticus* and some *Neisseria* species.

CONTRAINDICATIONS: Epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, and many other viral diseases of the cornea and conjunctiva. Mycobacterial infection of the eye. Fungal diseases of ocular structures. Hypersensitivity to a component of the medication.

WARNINGS:

FOR TOPICAL OPHTHALMIC USE. **NOT FOR INJECTION INTO THE EYE.** Sensitivity to topically applied aminoglycosides may occur in some patients. Severity of hypersensitivity reactions may vary from local effects to generalized reactions such erythema, itching, urticaria, skin rash, anaphylaxis, anaphylactoid reactions, or bullous reactions. If a sensitivity reaction does occur, discontinue use.

Prolonged use of steroids may result in glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision, and posterior subcapsular cataract formation. Intraocular pressure (IOP) should be routinely monitored even though it may be difficult in pediatric patients and uncooperative patients. Prolonged use may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions and parasitic infections of the eye, steroids may mask infection or enhance existing infection. In those diseases causing thinning of the cornea or sclera,

perforations have been known to occur with the use of topical steroids.

PRECAUTIONS:

General: The possibility of fungal infections of the cornea should be considered after long-term steroid dosing. As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be initiated. 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.

Cross-sensitivity to other aminoglycoside antibiotics may occur; if hypersensitivity develops with this product, discontinue use and institute appropriate therapy.

Ophthalmic ointment may retard corneal wound healing.

Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial ocular infection.

Information for Patients: Do not touch tube tip to any surface, as this may contaminate the contents. Contact lenses should not be worn during the use of this product.

Do not use the product if the imprinted carton seals have been damaged, or removed.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No studies have been conducted to evaluate the carcinogenic or mutagenic potential. No impairment of fertility was noted in studies of subcutaneous tobramycin in rats at doses of 50 and 100 mg/kg/day.

Pregnancy: Corticosteroids have been found to be teratogenic in animal studies. Ocular administration of 0.1% dexamethasone resulted in 15.6% and 32.3% incidence of fetal anomalies in two groups of pregnant rabbits. Fetal growth retardation and increased mortality rates have been observed in rats with chronic dexamethasone therapy. Reproduction studies have been performed in rats and rabbits with tobramycin at doses up to 100 mg/kg/day parenterally and have revealed no evidence of impaired fertility or harm to the fetus.

There are no adequate and well-controlled studies in pregnant women. However, prolonged or repeated corticoid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation. TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human

milk. Because many drugs are excreted in human milk, caution should be exercised when TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment) is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 2 years have not been established.

Geriatric Use: No overall clinical differences in safety or effectiveness have been observed between the elderly and other adult patients.

ADVERSE REACTIONS: Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination. Exact incidence figures are not available.

The most frequent adverse reactions to topical ocular tobramycin [TOBREX® (tobramycin ophthalmic ointment) 0.3%] are hypersensitivity and localized ocular toxicity, including lid itching and swelling, and conjunctival erythema. These reactions occur in less than 4% of patients.

The reactions due to the steroid component are: elevation of intraocular pressure with possible development of glaucoma, and infrequent optic nerve damage; posterior subcapsular cataract formation; and delayed wound healing.

Secondary Infection. The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroids. The possibility of fungal invasion must be considered in any persistent corneal ulceration where steroid treatment has been used. Secondary bacterial ocular infection following suppression of host responses also occurs.

Postmarketing Experience: Additional adverse reactions identified from postmarketing use include, anaphylactic reaction, erythema multiforme.

The following additional adverse reactions have been reported with the individual components listed below:

Dexamethasone: Cushing’s syndrome and adrenal suppression may occur after use of dexamethasone in excess of the listed dosing instructions in predisposed patients, including children and patients treated with CYP3A4 inhibitors.

Aminoglycosides: Neurotoxicity, ototoxicity, and nephrotoxicity have occurred in patients receiving systemic aminoglycoside therapy. Aminoglycosides may aggravate muscle weakness in patients with known or suspected neuromuscular disorders, such as myasthenia gravis or Parkinson’s disease, because of their potential effect on neuromuscular function.

DOSAGE AND ADMINISTRATION: Apply a small amount (approximately ½ inch ribbon) into the conjunctival sac(s) up to three or four times daily.

How to apply TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment):

1. Tilt your head back.

2. Place a finger on your cheek just under your eye and gently pull down until a "V" pocket is formed between your eyeball and your lower lid.

3. Place a small amount (about ½ inch) of TOBRADEX® (tobramycin and dexamethasone ophthalmic ointment). Do not let the tip of the tube touch your eye.

4. Look downward before closing your eye.

Not more than 8 g should be prescribed initially and the prescription should not be refilled without further evaluation as outlined in PRECAUTIONS above.

HOW SUPPLIED: 3.5 g STERILE ointment supplied in an aluminum tube with a white polyethylene tip and white polyethylene cap (NDC 0078-0876-01)

STORAGE: Store at 2°C to 25°C (36°F to 77°F).

After opening, TOBRADEX (tobramycin and dexamethasone ophthalmic ointment) can be used until the expiration date on the tube.

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

T2021-62

May 2021

PRINCIPAL DISPLAY PANEL

NDC 0078-0876-01

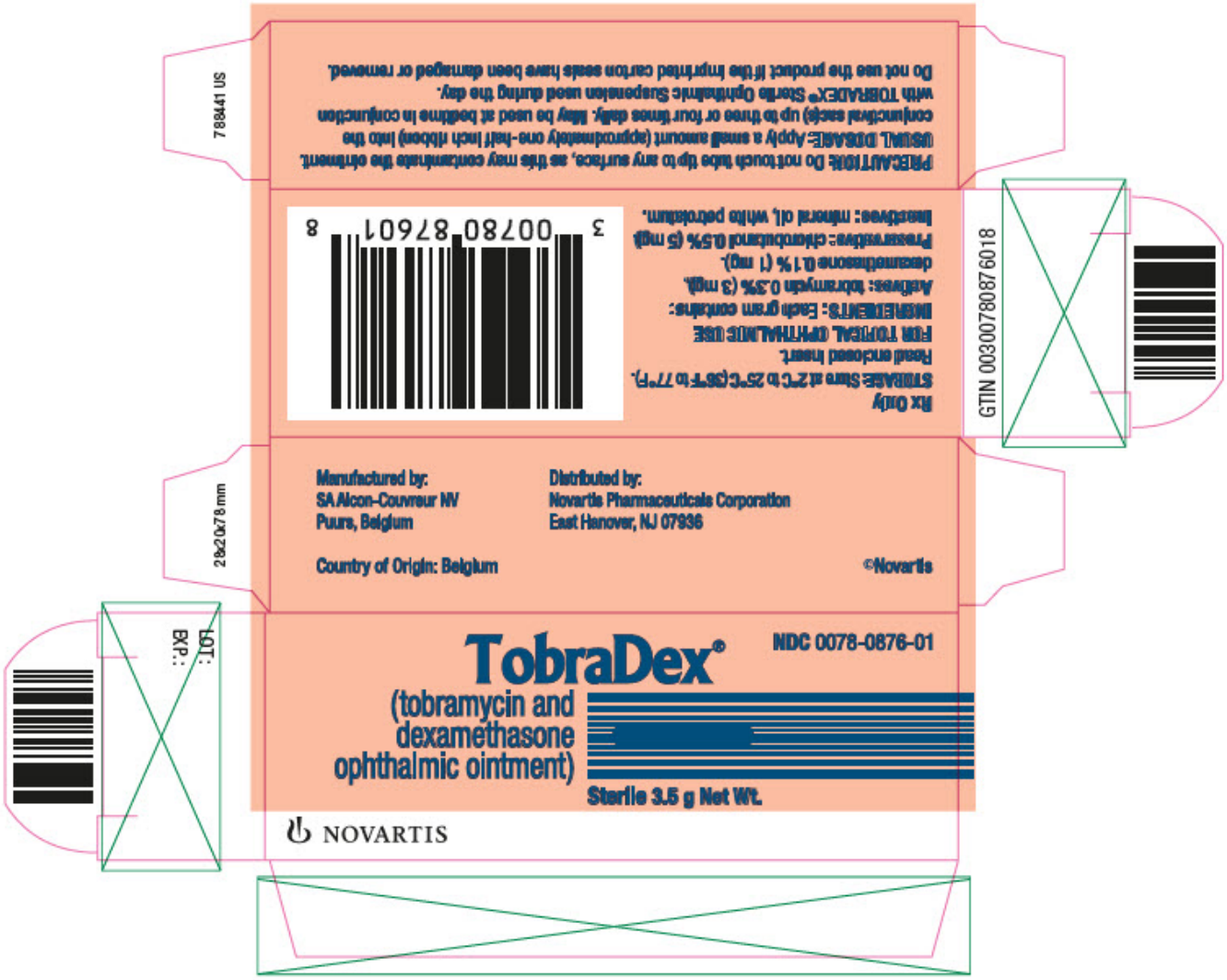
TobraDex®

(tobramycin and dexamethasone ophthalmic ointment)

Sterile 3.5 g Net Wt.

Rx Only

NOVARTIS



TOBRADEX

tobramycin and dexamethasone ointment

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0078-0876
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TOBRAMYCIN (UNII: VZ8RRZ51VK) (TOBRAMYCIN - UNII:VZ8RRZ51VK)	TOBRAMYCIN	3 mg in 1 g
DEXAMETHASONE (UNII: 7S5I7G3JQL) (DEXAMETHASONE - UNII:7S5I7G3JQL)	DEXAMETHASONE	1 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
CHLOROBUTANOL (UNII: HM4YQM8WRC)	
MINERAL OIL (UNII: T5L8T28FGP)	

PETROLATUM (UNII: 4T6H12BN9U)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0078-0876-01	3.5 g in 1 TUBE; Type 0: Not a Combination Product	10/27/2020	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA050616	10/15/1988	

Labeler - Novartis Pharmaceuticals Corporation (002147023)

Revised: 8/2023 Novartis Pharmaceuticals Corporation