TOBRAMYCIN AND DEXAMETHASONE- tobramycin and dexamethasone suspension/ drops
Amneal Pharmaceuticals NY LLC

Tobramycin and Dexamethasone Ophthalmic Suspension, USP
Sterile

DESCRIPTION

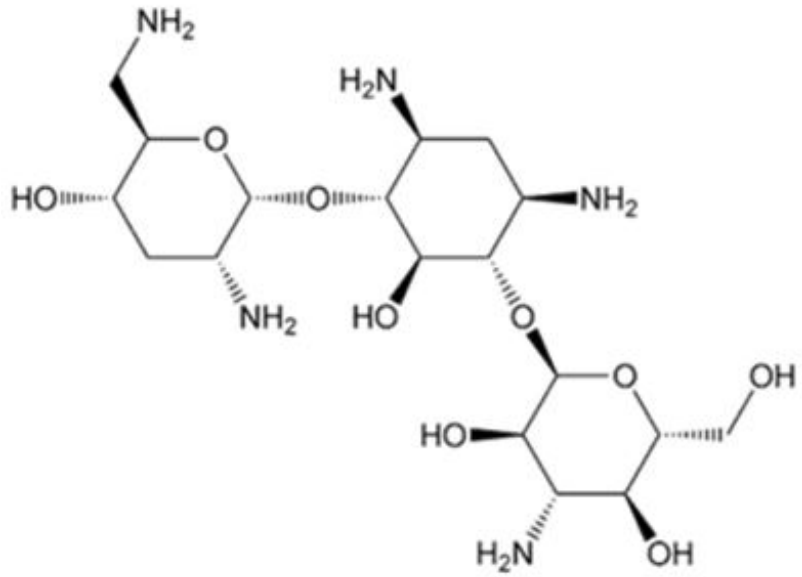
Tobramycin and dexamethasone ophthalmic suspension, USP is a sterile, multiple-dose antibiotic and steroid combination for topical ophthalmic use.

The chemical structures for tobramycin and dexamethasone are presented below:

Tobramycin, USP

Tobramycin, USP is a white to off-white, hygroscopic powder. It is freely soluble in water, very slightly soluble in alcohol, practically insoluble in chloroform and in ether.

Chemical Structure:

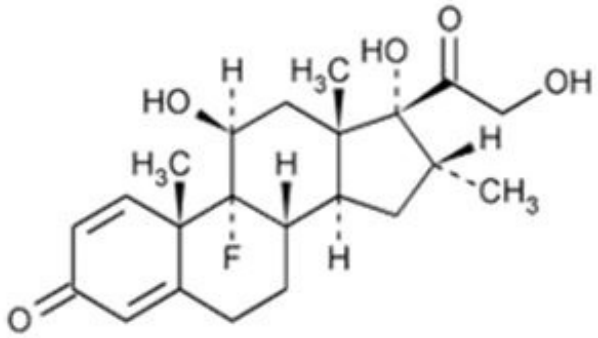


Molecular Formula: $C_{18}H_{37}N_5O_9$
Molecular Weight: 467.51
Chemical Name: *O*-3-Amino-3-deoxy-α-D-glucopyranosyl-(1→4)-O-[2,6-diamino-2,3,6-trideoxy-α-D-*ribo*-hexopyranosyl (1→6)]-2-deoxy-L-streptamine

Dexamethasone, USP

Dexamethasone, USP (Micronised) is a white or practically white crystalline powder.

Chemical Structure:



Molecular Formula: $C_{22}H_{29}FO_5$
Molecular Weight: 392.46
Chemical Name: 9-Fluoro-11ß,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione

Each mL of tobramycin and dexamethasone ophthalmic suspension, USP contains:

Active: tobramycin, USP 0.3% (3 mg) and dexamethasone, USP 0.1% (1 mg).

Preservative: benzalkonium chloride 0.01%.

Inactives: tyloxapol, edetate disodium, sodium chloride, hydroxyethyl cellulose, sodium sulfate, sulfuric acid and/or sodium hydroxide (to adjust pH) and water for injection, USP.

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 tobramycin and dexamethasone ophthalmic suspension; however, it is known that some systemic absorption can occur with ocularly applied drugs.

INDICATIONS AND USAGE

Tobramycin and dexamethasone ophthalmic suspension 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 as 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.

Information for Patients

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

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. Tobramycin and dexamethasone ophthalmic suspension 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 tobramycin and dexamethasone ophthalmic suspension 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 differences in safety or effectiveness have been observed between elderly and younger 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 (tobramycin ophthalmic solution, 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 IOP 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.

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

One or two drops instilled into the conjunctival sac(s) every four to six hours. During the initial 24 to 48 hours, the dosage may be increased to one or two drops every two (2) hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

Not more than 20 mL should be prescribed initially and the prescription should not be refilled without further evaluation as outlined in **PRECAUTIONS** above.

HOW SUPPLIED

Tobramycin and Dexamethasone Ophthalmic Suspension USP, **0.3% and 0.1%** is a sterile, white to off-white uniform suspension, essentially free from foreign matter, supplied in 2.5 mL 5 mL or 10 mL LDPE natural bottle with LDPE natural nozzle and HDPE white cap. Each mL contains tobramycin, USP 0.3% (3 mg) and dexamethasone, USP 0.1% (1 mg).

It is available as follows:

2.5 mL in 5 mL Container:	NDC 69238-1373-2
5 mL in 5 mL Container:	NDC 69238-1374-3
10 mL in 10 mL Container:	NDC 69238-1375-6

STORAGE

Store at 8º to 27ºC (46º to 80ºF).

Store suspension upright and shake well before using.

After opening, tobramycin and dexamethasone ophthalmic suspension can be used until the expiration date on the bottle.

Manufactured by:
Amneal Pharmaceuticals Pvt. Ltd.
Parenteral Unit
Ahmedabad 382213, INDIA

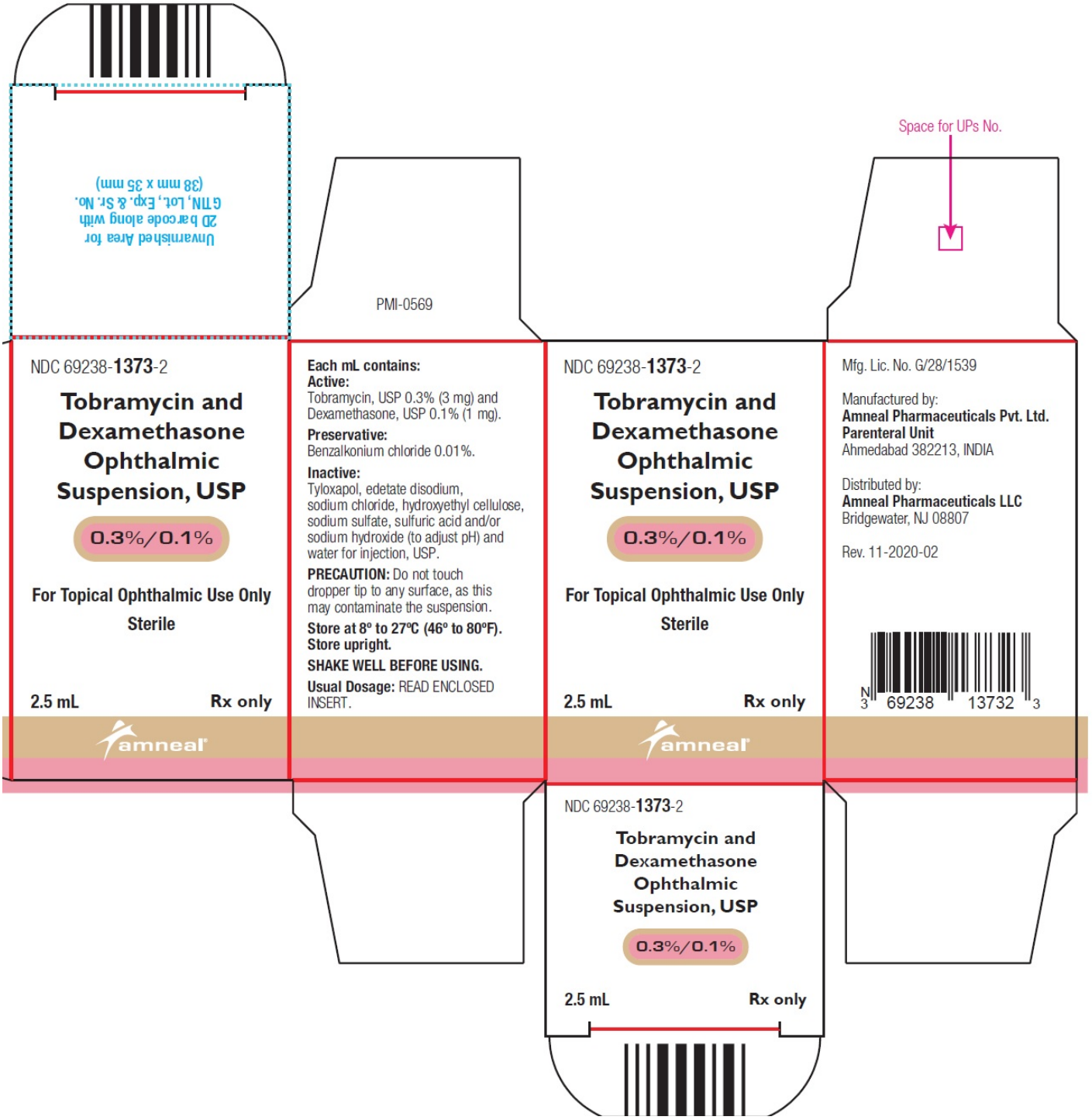
Distributed by:
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

Rev. 05-2021-05

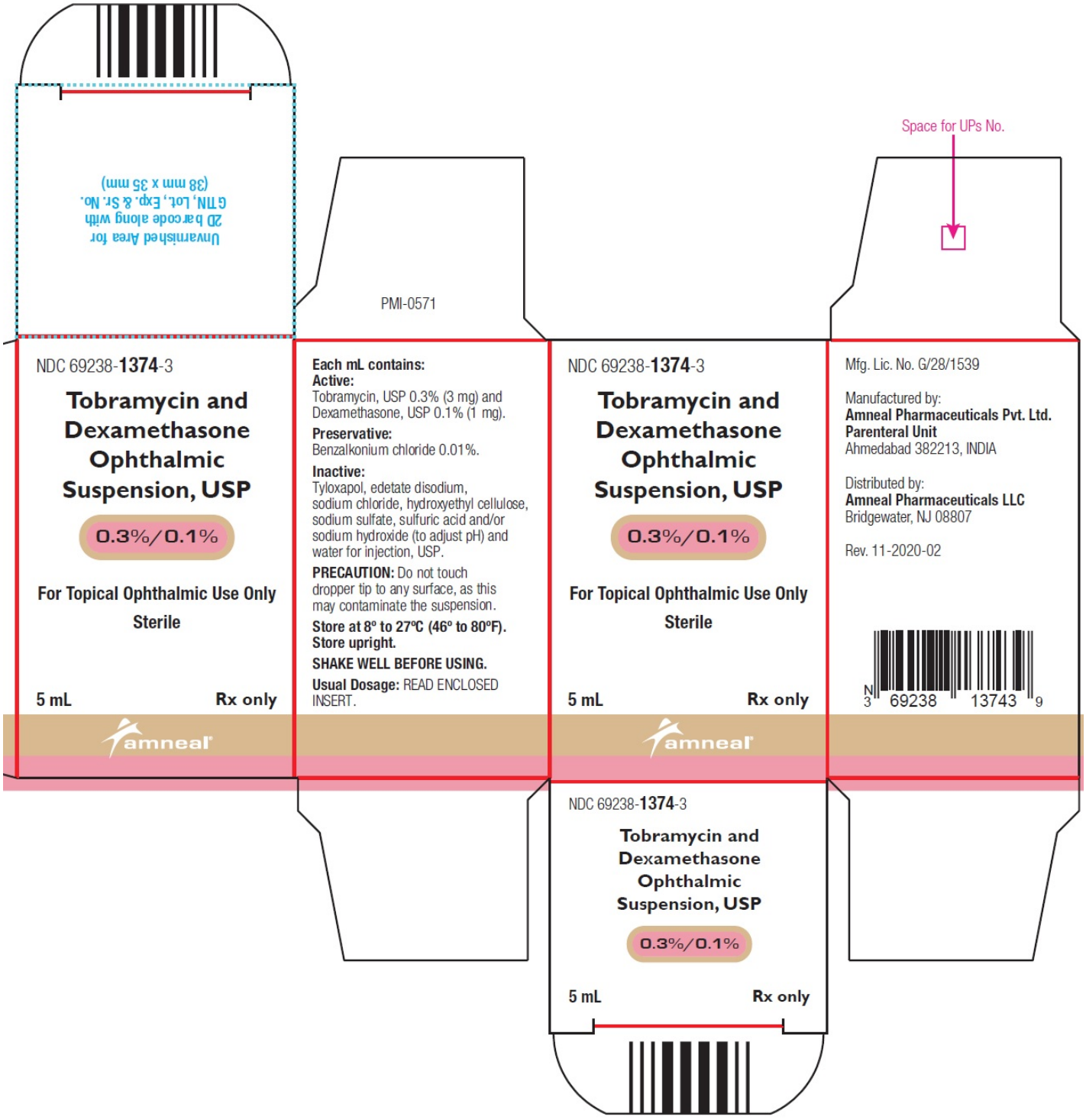
PRINCIPAL DISPLAY PANEL

NDC 69238-1373-2
Tobramycin and Dexamethasone Ophthalmic Solution USP, 0.3%/0.1%
Rx Only
2.5 mL
Amneal Pharmaceuticals LLC


Unvarnished Area for, (6 x 14 mm)
NDC 69238-1373-2
Tobramycin and Dexamethasone Ophthalmic Suspension, USP
0.3%/0.1%
For Topical Ophthalmic Use Only
Sterile
2.5 mL
Rx only
Each mL contains:
Active: Tobramycin, USP 0.3% (3 mg) and Dexamethasone, USP 0.1% (1 mg).
Preservative: Benzalkonium chloride 0.01%. Inactive: Tyloxapol, edetate disodium, sodium chloride, hydroxyethyl cellulose, sodium sulfate, sulfuric acid and/or sodium hydroxide (to adjust pH) and water for injection, USP.
PRECAUTION: Do not touch dropper tip to any surface, as this may contaminate the suspension.
Store at 8° to 27°C (46° to 80°F). Store upright.
SHAKE WELL BEFORE USING.
Usual Dosage: READ ENCLOSED INSERT.
Mfg. Lic. No. G/28/1539
Distributed by:
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807
Rev. 11-2021-03 Made in INDIA
Unvarnished Area for, Lot. & Exp. (10 x 14 mm)


Unvarnished Area for 2D barcode along with GTIN, Lot., Exp. & Sr. No. (38 mm x 35 mm)
PMI-0569
Space for UPs No.
NDC 69238-1373-2
Tobramycin and Dexamethasone Ophthalmic Suspension, USP
0.3%/0.1%
For Topical Ophthalmic Use Only
Sterile
2.5 mL
Rx only
amneal
Each mL contains:
Active:
Tobramycin, USP 0.3% (3 mg) and Dexamethasone, USP 0.1% (1 mg).
Preservative:
Benzalkonium chloride 0.01%.
Inactive:
Tyloxapol, edetate disodium, sodium chloride, hydroxyethyl cellulose, sodium sulfate, sulfuric acid and/or sodium hydroxide (to adjust pH) and water for injection, USP.
PRECAUTION: Do not touch dropper tip to any surface, as this may contaminate the suspension.
Store at 8° to 27°C (46° to 80°F). Store upright.
SHAKE WELL BEFORE USING.
Usual Dosage: READ ENCLOSED INSERT.
NDC 69238-1373-2
Tobramycin and Dexamethasone Ophthalmic Suspension, USP
0.3%/0.1%
For Topical Ophthalmic Use Only
Sterile
2.5 mL
Rx only
amneal
Mfg. Lic. No. G/28/1539
Manufactured by:
Amneal Pharmaceuticals Pvt. Ltd.
Parenteral Unit
Ahmedabad 382213, INDIA
Distributed by:
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807
Rev. 11-2020-02
N 3 69238 13732 3
NDC 69238-1373-2
Tobramycin and Dexamethasone Ophthalmic Suspension, USP
0.3%/0.1%
2.5 mL
Rx only

NDC 69238-1374-3
Tobramycin and Dexamethasone Ophthalmic Solution USP, 0.3%/0.1%
Rx Only
5 mL
Amneal Pharmaceuticals LLC



NDC 69238-1375-6
Tobramycin and Dexamethasone Ophthalmic Solution USP, 0.3%/0.1%
Rx Only
10 mL
Amneal Pharmaceuticals LLC

Unvarnished Area for
(6 mm x 18 mm)

NDC 69238-1375-6

Tobramycin and Dexamethasone Ophthalmic Suspension, USP

0.3%/0.1%

For Topical Ophthalmic Use Only
Sterile

10 mL

Rx only

Each mL contains:
Active: Tobramycin, USP 0.3% (3 mg) and Dexamethasone, USP 0.1% (1 mg).
Preservative: Benzalkonium chloride 0.01%. **Inactive:** Tyloxapol, edetate disodium, sodium chloride, hydroxyethyl cellulose, sodium sulfate, sulfuric acid and/or sodium hydroxide (to adjust pH) and water for injection, USP.
PRECAUTION: Do not touch dropper tip to any surface, as this may contaminate the suspension.
Store at 8° to 27°C (46° to 80°F). Store upright.
SHAKE WELL BEFORE USING.
Usual Dosage:
READ ENCLOSED INSERT.
Mfg. Lic. No. G/28/1539
Distributed by:
Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807
Rev. 11-2021-03 Made in INDIA

Unvarnished Area for
Lot. and Exp.
(10 mm x 18 mm)

TOBRAMYCIN AND DEXAMETHASONE

tobramycin and dexamethasone suspension/ drops

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69238-1373
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 mL
DEXAMETHASONE (UNII: 7S5I7G3JQL) (DEXAMETHASONE - UNII:7S5I7G3JQL)	DEXAMETHASONE	1 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
HYDROXYETHYL CELLULOSE (2000 CPS AT 1%) (UNII: S38J6RZN16)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SODIUM SULFATE (UNII: 0YPR65R21J)	
SULFURIC ACID (UNII: O40UQP6WCF)	
TYLOXAPOL (UNII: Y27PUL9H56)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	white (white to off-white uniform suspension)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69238-1373-2	1 in 1 CARTON	07/17/2021	
1		2.5 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212991	07/17/2021	

TOBRAMYCIN AND DEXAMETHASONE

tobramycin and dexamethasone suspension/ drops

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69238-1374
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 mL
DEXAMETHASONE (UNII: 7S5I7G3JQL) (DEXAMETHASONE - UNII:7S5I7G3JQL)	DEXAMETHASONE	1 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
HYDROXYETHYL CELLULOSE (2000 CPS AT 1%) (UNII: S38J6RZN16)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SODIUM SULFATE (UNII: 0YPR65R21J)	
SULFURIC ACID (UNII: O40UQP6WCF)	
TYLOXAPOL (UNII: Y27PUL9H56)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics			
Color	white (white to off-white uniform suspension)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:69238-1374-3	1 in 1 CARTON	07/17/2021	
1		5 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212991	07/17/2021	

TOBRAMYCIN AND DEXAMETHASONE

tobramycin and dexamethasone suspension/ drops

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69238-1375
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 mL
DEXAMETHASONE (UNII: 7S5I7G3JQL) (DEXAMETHASONE - UNII:7S5I7G3JQL)	DEXAMETHASONE	1 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
HYDROXYETHYL CELLULOSE (2000 CPS AT 1%) (UNII: S38J6RZN16)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SODIUM SULFATE (UNII: 0YPR65R21J)	
SULFURIC ACID (UNII: O40UQP6WCF)	
TYLOXAPOL (UNII: Y27PUL9H56)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	white (white to off-white uniform suspension)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69238-1375-6	1 in 1 CARTON	07/17/2021	
1		10 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212991	07/17/2021	

Labeler - Amneal Pharmaceuticals NY LLC (123797875)

Revised: 12/2023 Amneal Pharmaceuticals NY LLC