

NEOMYCIN AND POLYMYXIN B SULFATES, BACITRACIN ZINC AND HYDROCORTISONE- neomycin sulfate and polymyxin b sulfate, bacitracin zinc and hydrocortisone ointment
MWI/VetOne

Neomycin and Polymyxin B Sulfates, Bacitracin Zinc and Hydrocortisone Ophthalmic Ointment, USP
(Sterile)

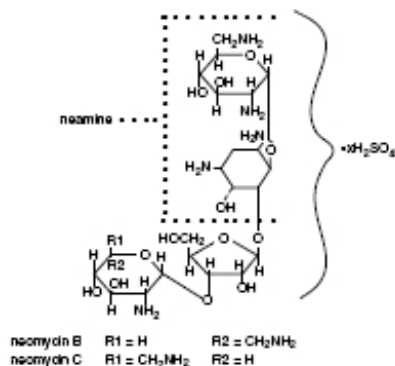
DESCRIPTION:

Neomycin and Polymyxin B Sulfates, Bacitracin Zinc and Hydrocortisone Ophthalmic Ointment, USP is a sterile antimicrobial and anti-inflammatory ointment for ophthalmic use.

Each Gram Contains: ACTIVES: Neomycin sulfate (equivalent to 3.5 mg neomycin base), Polymyxin B Sulfate equivalent to 10,000 polymyxin B units, Bacitracin Zinc equivalent to 400 bacitracin units, Hydrocortisone 10 mg (1%); INACTIVES: White Petrolatum, Mineral Oil.

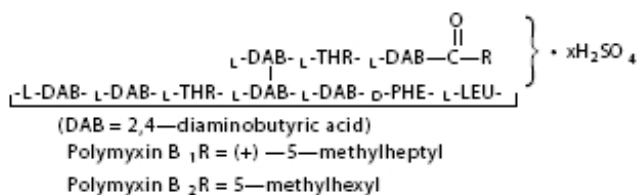
Neomycin sulfate is the sulfate salt of neomycin B and C, which are produced by the growth of *Streptomyces fradiae* Waksman (Fam. Streptomycetaceae). It has a potency equivalent of not less than 600 mcg of neomycin standard per mg, calculated on an anhydrous basis.

The structural formulae are:



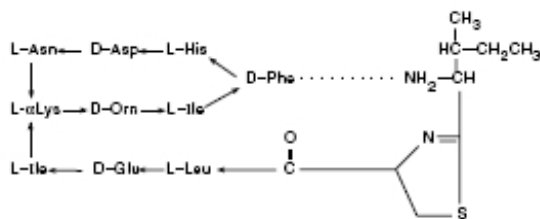
Polymyxin B sulfate is the sulfate salt of polymyxin B₁ and B₂, which are produced by the growth of *Bacillus polymyxa* (Prazmowski) Migula (Fam. Bacillaceae). It has a potency of not less than 6,000 polymyxin B units per mg, calculated on an anhydrous basis.

The structural formulae are:



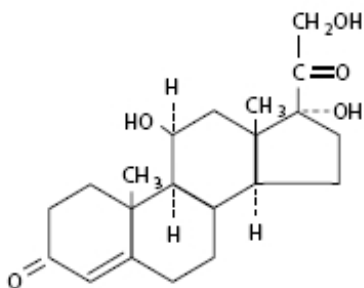
Bacitracin zinc is the zinc salt of bacitracin, a mixture of related cyclic polypeptides (mainly bacitracin A) produced by the growth of an organism of the *licheniformis* group of *Bacillus subtilis* var Tracy. It has a potency of not less than 40 bacitracin units per mg.

The structural formula is:



Hydrocortisone, 11 β , 17, 21-trihydroxypregn-4-ene-3, 20-dione, is an anti-inflammatory hormone.

Its structural formula is:



CLINICAL PHARMACOLOGY:

Corticosteroids suppress the inflammatory response to a variety of agents and they probably delay or slow healing. Since corticosteroids may inhibit the body's defense mechanism against infection, concomitant antimicrobial drugs may be used when this inhibition is considered to be clinically significant in a particular case.

When a decision to administer both a corticosteroid and antimicrobials is made, the administration of such drugs in combination has the advantage of greater patient compliance and convenience, with the added assurance that the appropriate dosage of all drugs is administered. When each type of drug is in the same formulation, compatibility of ingredients is assured and the correct volume of drug is delivered and retained.

The relative potency of corticosteroids depends on the molecular structure, concentration and release from the vehicle.

Microbiology:

The anti-infective components in neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment are included to provide action against specific organisms susceptible to it. Neomycin sulfate and polymyxin B sulfate are active *in vitro* against susceptible strains of the following microorganisms: *Staphylococcus aureus*, streptococci, including *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella-Enterobacter* species, *Neisseria* species, and *Pseudomonas aeruginosa*. This product does not provide adequate coverage against *Serratia marcescens* (see INDICATIONS AND USAGE).

INDICATIONS AND USAGE:

Neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial infection exists.

Ocular corticosteroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe where the inherent risk of corticosteroid use in certain infective conjunctivitis 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 infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye (see CLINICAL PHARMACOLOGY: Microbiology).

The particular anti-infective drugs in this product are active against the following common bacterial eye pathogens: *Staphylococcus aureus*, streptococci, including *Streptococcus pneumoniae*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella-Enterobacter* species, *Neisseria* species, and *Pseudomonas aeruginosa*. The product does not provide adequate coverage against *Serratia marcescens*.

CONTRAINDICATIONS:

Neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment is contraindicated in most viral diseases of the cornea and conjunctiva including: epithelial herpes simplex keratitis (dendritic keratitis), vaccinia and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

This product is also contraindicated in individuals who have shown hypersensitivity to any of its components. Hypersensitivity to the antibiotic component occurs at a higher rate than for other components.

WARNINGS:

NOT FOR INJECTION INTO THE EYE. Neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment should never be directly introduced into the anterior chamber of the eye. Ophthalmic ointments may retard corneal wound healing. Prolonged use of corticosteroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation.

Prolonged use may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids. In acute purulent conditions of the eye, corticosteroids may mask infection or enhance existing infection.

If these products are used for 10 days or longer, intraocular pressure should be routinely monitored even though it may be difficult in uncooperative patients. Corticosteroids should be used with caution in the presence of glaucoma.

The use of corticosteroids after cataract surgery may delay healing and increase the incidence of filtering blebs.

Use of ocular corticosteroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Employment of corticosteroid medication in the treatment of herpes simplex requires great caution.

Topical antibiotics, particularly neomycin sulfate, may cause cutaneous sensitization. A precise incidence of hypersensitivity reactions (primarily skin rash) due to topical antibiotics is not known. The

manifestations of sensitization to topical antibiotics are usually itching, reddening, and edema of the conjunctiva and eyelid. A sensitization reaction may manifest simply as a failure to heal. During long-term use of topical antibiotic products, periodic examination for such signs is advisable, and the patient should be told to discontinue the product if they are observed. Symptoms usually subside quickly on withdrawing the medication. Applications of products containing these ingredients should be avoided for the patient thereafter (see PRECAUTIONS: General).

PRECAUTIONS:

General:

The initial prescription and renewal of the medication order beyond 8 grams should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

The possibility of fungal infections of the cornea should be considered after prolonged corticosteroid dosing. Fungal cultures should be taken when appropriate.

If this product is used for 10 days or longer, intraocular pressure should be monitored (see WARNINGS).

There have been reports of bacterial keratitis associated with the use of topical ophthalmic products in multiple-dose containers which have been inadvertently contaminated by patients, most of whom had a concurrent corneal disease or a disruption of the ocular epithelial surface (see PRECAUTIONS: Information for Patients).

Allergic cross-reactions may occur which could prevent the use of any or all of the following antibiotics for the treatment of future infections: kanamycin, paromomycin, streptomycin, and possibly gentamicin.

Information for Patients:

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, eyelid, fingers, or any other surface. The use of this product by more than one person may spread infection.

Patients should also be instructed that ocular products, if handled improperly, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated products (see PRECAUTIONS: General).

If the condition persists or gets worse, or if a rash or allergic reaction develops, the patient should be advised to stop use and consult a physician. Do not use this product if you are allergic to any of the listed ingredients.

Keep tightly closed when not in use. Keep out of the reach of children.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long-term studies in animals to evaluate carcinogenic or mutagenic potential have not been conducted with polymyxin B sulfate or bacitracin. Treatment of cultured human lymphocytes *in vitro* with neomycin increased the frequency of chromosome aberrations at the highest concentration (80 mcg /mL) tested; however, the effects of neomycin on carcinogenesis and mutagenesis in humans are unknown.

Long-term studies in animals (rats, rabbits, mice) showed no evidence of carcinogenicity or mutagenicity attributable to oral administration of corticosteroids. Long-term animal studies have not been performed to evaluate the carcinogenic potential of topical corticosteroids. Studies to determine mutagenicity with hydrocortisone have revealed negative results.

Polymyxin B has been reported to impair the motility of equine sperm, but its effects on male or female fertility are unknown. No adverse effects on male or female fertility, litter size or survival were observed in rabbits given bacitracin zinc 100 gm/ton of diet. Long-term animal studies have not been performed to evaluate the effect on fertility of topical corticosteroids.

Pregnancy:

Teratogenic Effects:

Pregnancy Category C. Corticosteroids have been found to be teratogenic in rabbits when applied topically at concentrations of 0.5% on days 6 to 18 of gestation and in mice when applied topically at a concentration of 15% on days 10 to 13 of gestation. There are no adequate and well-controlled studies in pregnant women. Neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Because of the potential for serious adverse reactions in nursing infants from neomycin and polymyxin B sulfates, bacitracin zinc and hydrocortisone ophthalmic ointment, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS:

Adverse reactions have occurred with corticosteroid/anti-infective combination drugs which can be attributed to the corticosteroid component, the anti-infective component, or the combination. The exact incidence is not known.

Reactions occurring most often from the presence of the anti-infective ingredient are allergic sensitization reactions including itching, swelling and conjunctival erythema (see WARNINGS). More serious hypersensitivity reactions, including anaphylaxis, have been reported rarely.

The reactions due to the corticosteroid component in decreasing order of frequency are: elevation of intraocular pressure (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 corticosteroids and antimicrobials. Fungal and viral infections of the cornea are particularly prone to develop coincidentally with long-term applications of a corticosteroid. The possibility of fungal invasion must be considered in any persistent corneal ulceration where corticosteroid treatment has been used.

Local irritation on instillation has also been reported.

DOSAGE AND ADMINISTRATION:

Apply the ointment in the affected eye every 3 or 4 hours, depending on the severity of the condition.

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

HOW SUPPLIED:

Neomycin and Polymyxin B Sulfates, Bacitracin Zinc and Hydrocortisone Ophthalmic Ointment, USP is supplied in a tube with ophthalmic tip applicator in the following size:

3.5 g - Prod. No. 03934.

DO NOT USE IF CAP AND NECKRING ARE NOT INTACT.

FOR OPHTHALMIC USE ONLY

Storage:

Store between 15° - 30°C (59° - 86°F).

KEEP OUT OF REACH OF CHILDREN.

Rx only

Revised November 2007

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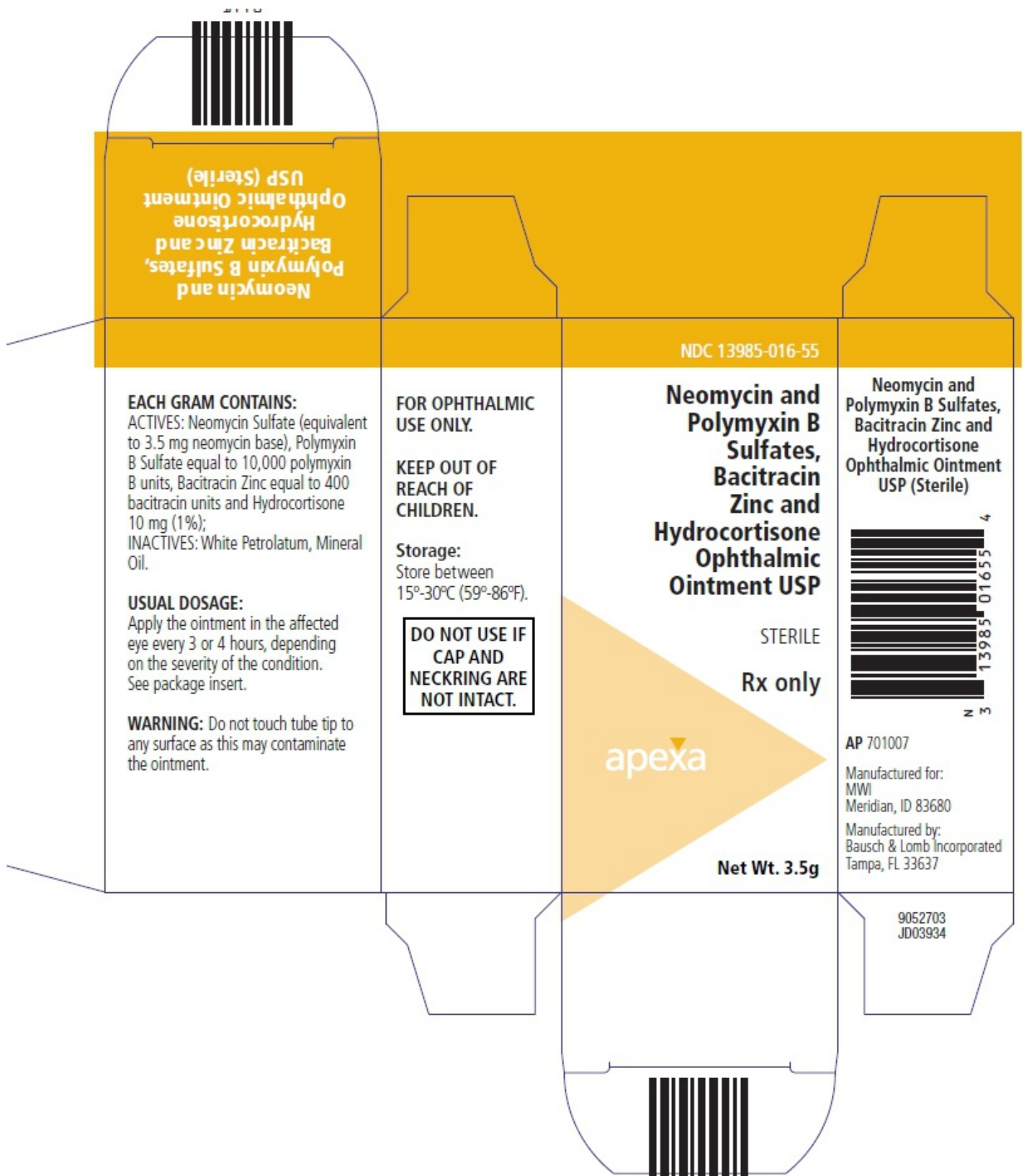
Tampa, FL 33637

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9113900 **(Flat)**

Principal Display Panel



NDC 13985-016-55

Neomycin and Polymyxin B Sulfates, Bacitracin Zinc and Hydrocortisone Ophthalmic Ointment USP

STERILE

Rx only

apexa

Net Wt. 3.5g

NEOMYCIN AND POLYMYXIN B SULFATES, BACITRACIN ZINC AND HYDROCORTISONE

neomycin sulfate and polymyxin b sulfate, bacitracin zinc and hydrocortisone ointment

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:13985-016
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
NEOMYCIN SULFATE (UNII: 057Y626693) (NEOMYCIN - UNII:H6QD7X297)	NEOMYCIN SULFATE	3.5 mg in 1 g
POLYMYXIN B SULFATE (UNII: 19371312D4) (POLYMYXIN B - UNII:J2VZ07J96K)	POLYMYXIN B SULFATE	10000 [USP'U] in 1 g
BACITRACIN ZINC (UNII: 89Y4M234ES) (BACITRACIN - UNII:58H6RWO52I)	BACITRACIN ZINC	400 [USP'U] in 1 g
HYDROCORTISONE (UNII: W14X0X7BPJ) (HYDROCORTISONE - UNII:W14X0X7BPJ)	HYDROCORTISONE	10 mg in 1 g

Inactive Ingredients	
Ingredient Name	Strength
MINERAL OIL (UNII: T5L8T28FGP)	
PETROLATUM (UNII: 4T6H12BN9U)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13985-016-55	1 in 1 CARTON		
1		3.5 g in 1 TUBE		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA064068	10/30/1995	

Labeler - MWI/VetOne (019926120)

Registrant - Bausch & Lomb Incorporated (196603781)

Establishment			
Name	Address	ID/FEI	Business Operations
Bausch & Lomb Incorporated		807927397	MANUFACTURE

