

NEOMYCIN AND POLYMYXIN B SULFATES AND HYDROCORTISONE- neomycin sulfate, polymyxin b sulfate and hydrocortisone suspension/ drops
NuCare Pharmaceuticals, Inc.

Neomycin and Polymyxin B

Sulfates and Hydrocortisone

Otic Suspension, USP

(Sterile)

Rx only

DESCRIPTION

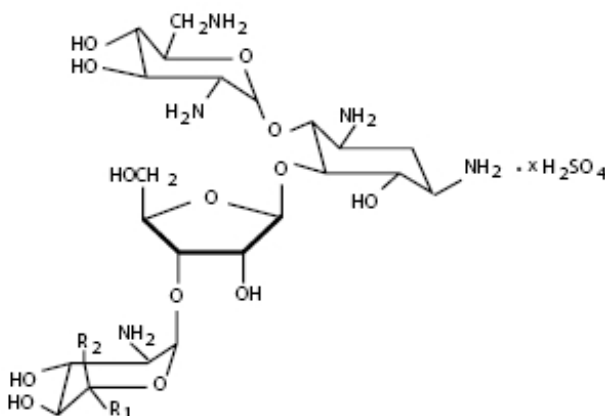
Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension USP, is a sterile antibacterial and anti-inflammatory suspension for otic use.

Each mL contains:

ACTIVES:Neomycin Sulfate equivalent to 3.5 mg neomycin base, Polymyxin B Sulfate, equal to 10,000 polymyxin B units, and Hydrocortisone, 10 mg (1%); **INACTIVES:**Cetyl Alcohol (0.9%), Polysorbate 80, Propylene Glycol, Purified Water. Sulfuric Acid may be added to adjust pH (3.0 - 7.0).

PRESERVATIVE ADDED:Thimerosal 0.01%.

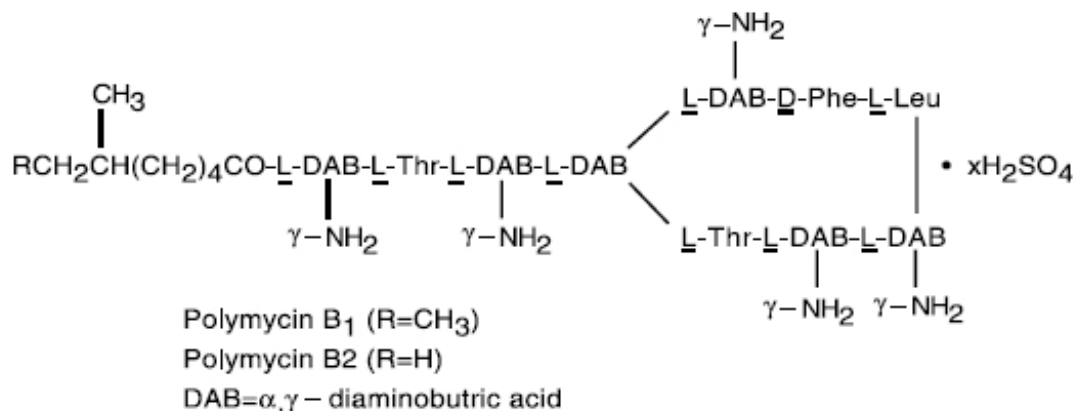
Neomycin sulfate is the sulfate salt of neomycin B and C, which are produced by the growth of *Streptomyces fradiae* Waksman (Fam. Streptomycetaceae). It has a potency equivalent to not less than 600 micrograms of neomycin standard per milligram, calculated on an anhydrous basis. The structural formulae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



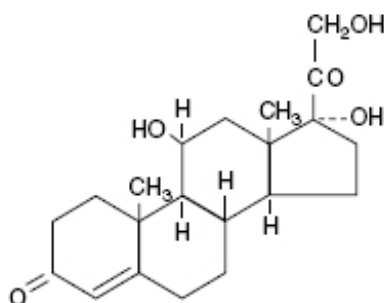
Neomycin B ($R_1 = H$, $R_2 = CH_2NH_2$)
Neomycin C ($R_1 = CH_2NH_2$, $R_2 = H$)

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 milligram, calculated on an anhydrous basis. The structural formulae are:



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



C₂₁H₃₀O₅

Mol. Wt. 362.46

CLINICAL PHARMACOLOGY

Corticoids suppress the inflammatory response to a variety of agents and they may delay 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 in a particular case.

The anti-infective components in the combination are included to provide action against specific organisms susceptible to them. Neomycin sulfate and polymyxin B sulfate together are considered active against the following microorganisms: *Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella-Enterobacter* species, *Neisseria* species and *Pseudomonas aeruginosa*. This product does not provide adequate coverage against *Serratia marcescens* and streptococci, including *Streptococcus pneumoniae*.

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

INDICATIONS AND USAGE

For the treatment of superficial bacterial infections of the external auditory canal caused by organisms susceptible to the action of the antibiotics, and for the treatment of infections of mastoidectomy and fenestration cavities caused by organisms susceptible to the antibiotics.

CONTRAINDICATIONS

This product is contraindicated in those individuals who have shown hypersensitivity to any of its components, and in herpes simplex, vaccinia, and varicella infections.

WARNINGS

Neomycin can induce permanent sensorineural hearing loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti. The risk is greater with prolonged use. Therapy should be limited to 10 consecutive days (see PRECAUTIONS - General). Patients being treated with eardrops containing neomycin should be under close clinical observation. Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension should not be used in any patient with a perforated tympanic membrane.

Discontinue promptly if sensitization or irritation occurs.

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

When using neomycin-containing products to control secondary infection in the chronic dermatoses, such as chronic otitis externa or stasis dermatitis, it should be borne in mind that the skin in these conditions is more liable than is normal skin to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low-grade reddening with swelling, dry scaling, and itching; it may be manifested simply as a failure to heal. Periodic examination for such signs is advisable, and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for the patient thereafter.

PRECAUTIONS

General:

As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi.

If the infection is not improved after 1 week, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether therapy should be changed.

Treatment should not be continued for longer than 10 days.

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:

Avoid contaminating the bottle tip with material from the ear, fingers, or other source. This caution is necessary if the sterility of the drops is to be preserved.

If sensitization or irritation occurs, discontinue use immediately and contact your physician.

Do not use in the eyes.

SHAKE WELL BEFORE USING.**Laboratory Tests:**

Systemic effects of excessive levels of hydrocortisone may include a reduction in the number of circulating eosinophils and a decrease in urinary excretion of 17-hydroxycorticosteroids.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long-term studies in animals (rats, rabbits, mice) showed no evidence of carcinogenicity attributable to oral administration of corticosteroids.

Pregnancy:**Teratogenic effects:**

Pregnancy Category C. Corticosteroids have been shown 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. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

Hydrocortisone appears in human milk following oral administration of the drug. Since systemic absorption of hydrocortisone may occur when applied topically, caution should be exercised when Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension is used by a nursing woman.

Pediatric Use:

The safety and effectiveness of Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension in otitis externa have been established in the pediatric age group 2 years to 16 years of age. There is inadequate data to establish safety and effectiveness in otitis externa for pediatric patients under 2 years of age. ¹

Geriatric Use:

Clinical studies of Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

Neomycin occasionally causes skin sensitization. Ototoxicity and nephrotoxicity have also been reported (see WARNINGS). Adverse reactions have occurred with topical use of antibiotic combinations including neomycin and polymyxin B. Exact incidence figures are not available since no denominator of treated patients is available. The reaction occurring most often is allergic sensitization. In one clinical study, using a 20% neomycin patch, neomycin-induced allergic skin reactions occurred in two of 2,175 (0.09%) individuals in the general population. ² In another study, the incidence was found to be approximately 1%. ³

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

The following local adverse reactions have been reported with topical corticosteroids, especially under occlusive dressings: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria. Stinging and burning have been reported rarely when this drug has gained access to the middle ear.

DOSAGE AND ADMINISTRATION

Therapy with this product should be limited to 10 consecutive days.

The external auditory canal should be thoroughly cleansed and dried with a sterile cotton applicator.

For adults, 4 drops of the suspension should be instilled into the affected ear 3 to 4 times daily. For infants and children, 3 drops are suggested because of the smaller capacity of the ear canal.

The patient should lie with the affected ear upward and then the drops should be instilled. This position should be maintained for 5 minutes to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear.

If preferred, a cotton wick may be inserted into the canal and then the cotton may be saturated with the suspension. This wick should be kept moist by adding further suspension every 4 hours. The wick should be replaced at least once every 24 hours.

SHAKE WELL BEFORE USING.

HOW SUPPLIED

Neomycin and Polymyxin B Sulfates and Hydrocortisone Otic Suspension, USP is

supplied in a white plastic dropper bottle in the following size:

NDC 68071-4229-1 Bottles of 10 mL

Storage:

Store at 15°-25°C (59°-77°F).

Rx only

FOR USE IN EARS ONLY

DO NOT USE IF IMPRINTED NECKBAND IS NOT INTACT.

KEEP OUT OF REACH OF CHILDREN.

REFERENCES

1. Jones, RN, Milazzo J, Seidlin, M. Ofloxacin Otic Solution for Treatment of Otitis Externa in Children and Adults. *Arch Otolaryngol Head Neck Surg.* 1997; 123: 1193-1200.
2. Leyden JJ and Kligman AM. Contact dermatitis to neomycin sulfate. *JAMA.* 1979; 242: 1276-1278.
3. Prystowsky SD, Allen AM, Smith RW, Nonomura JH, Odom RB, Akers WA. Allergic contact hypersensitivity to nickel, neomycin, ethylenediamine, and benzocaine: relationships between age, sex, history of exposure, and reactivity to standard patch and use tests in a general population. *Arch Dermatol.* 1979; 115: 959-962.

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Revised: August 2016

9115704 (Flat)
9115604 (Folded)
Prod. No. 06509

Principal Display Panel

NuCare Pharmaceuticals, Inc.

Manufactured by: 3
 Bausch & Lomb Incorporated
 Bridgewater, NJ 08807
 Packaged By:
 NuCare Pharmaceuticals, Inc.
 Orange, CA 92867
 Patient Instructions:
 Instill _____ drops in the affected
 ear(s) _____ times a day.
 68071422901-10-00000-00000
 Rev 01/01/19

NDC: 68071-4229-1
Neo/Poly B Sulfates/Hc
10mL Otic Susp.

Each mL contains Actives: Neomycin Sulfate
 equivalent to 3.5mg Neomycin base, Polymyxin
 B Sulfate equal to 10,000 Polymyxin B units,
 and Hydrocortisone 10mg (1%)
 See manufacturer's label
 for full list of ingredients

Product #: R0304010
Rx Only

Neo/Poly B Sulfates/Hc
 Lot: 00000 NDC: 68071-4229-01
 MFR NDC: 24208-635-62 Exp.: 00-00
 Serial# 0000000002

Neo/Poly B Sulfates/Hc
 Lot: 00000 NDC: 68071-4229-01
 MFR NDC: 24208-635-62 Exp.: 00-00
 Serial# 0000000002



GTIN 00368071422917
 Serial# 0000000002
 Exp. Date 00-00
 LOT#: 00000

Call your doctor for medical advice about side
 effects. You may report side effects to FDA at
 1-800-FDA-1088.

WARNING: KEEP OUT OF REACH OF CHILDREN

STORE AT CONTROLLED TEMPERATURE 59-77°F.

NEOMYCIN AND POLYMYXIN B SULFATES AND HYDROCORTISONE

neomycin sulfate, polymyxin b sulfate and hydrocortisone suspension/ drops

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:68071-4229(NDC:24208- 635)
Route of Administration	AURICULAR (OTIC)		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDROCORTISONE (UNII: W4X0X7BPJ) (HYDROCORTISONE - UNII:W4X0X7BPJ)	HYDROCORTISONE	10 mg in 1 mL
NEOMYCIN SULFATE (UNII: 057Y626693) (NEOMYCIN - UNII:I16QD7X297)	NEOMYCIN	3.5 mg in 1 mL
POLYMYXIN B SULFATE (UNII: 19371312D4) (POLYMYXIN B - UNII:J2VZ 07J96K)	POLYMYXIN B	10000 [USP'U] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
CETYL ALCOHOL (UNII: 936JST6JCN)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
WATER (UNII: 059QF0KO0R)	
SULFURIC ACID (UNII: O40UQP6WCF)	
THIMEROSAL (UNII: 2225PI3MOV)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1	NDC:68071-4229-1	10 mL in 1 BOX; Type 0: Not a Combination Product	01/12/2018	
Marketing Information				
Marketing Category	Application Number or Monograph Citation		Marketing Start Date	Marketing End Date
ANDA	ANDA064065		08/28/1996	

Labeler - NuCare Pharmaceuticals,Inc. (010632300)

Establishment			
Name	Address	ID/FEI	Business Operations
NuCare Pharmaceuticals,Inc.		010632300	relabel(68071-4229)