Prescribing Information

PrNEOSPORIN®

Ointment

(Polymyxin B and Neomycin Sulfates, and Bacitracin zinc)

Antibacterial

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Prescribing Information

PrNEOSPORIN®

Ointment
(Polymyxin B and Neomycin Sulfates, and Bacitracin zinc)

Antibacterial

Clinical Pharmacology

The anti-infective components in the combination are included to provide action against specific organisms susceptible to them. Polymyxin B sulfate and neomycin sulfate together are considered active against the following microorganisms: *Staphylococcus aureus, Escherichia coli, Haemophilus influenzae, Klebsiella-Enterobacter* species, *Neisseria* species and *Pseudomonas aeruginosa*. Bacitracin is active against most Gram-positive bacteria, pathogenic *Neisseria spp* and *Haemophilus influenzae*.

Indications and Clinical Use

NEOSPORIN® (Neomycin and Polymyxin B Sulfates, and Bacitracin Zinc) Ointment is indicated for all lesions which are infected or likely to become infected by bacteria.

Contraindications

General

The use of NEOSPORIN® is contraindicated in patients who have demonstrated allergic hypersensitivity to any of the components of the preparation or to cross-sensitizing substances such as aminoglycosides and other related antibiotics.

Due to the known ototoxic and nephrotoxic potential of neomycin sulfate, the use of NEOSPORIN® in large quantities or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.

A possibility of increased absorption exists in very young children, thus NEOSPORIN® is not recommended for use in neonates and infants (<2 years). In neonates and infants, absorption by immature skin may be enhanced and renal function may be immature.

NEOSPORIN® (Neomycin and Polymyxin B Sulfates, and Bacitracin Zinc) Ointment should not be used in the eyes. It should not be used to treat otitis externa in the presence of a perforated tympanic membrane because of the risk of ototoxicity.

The presence of preexisting nerve deafness is a contraindication to the use of NEOSPORIN® (Neomycin and Polymyxin B Sulfates, and Bacitracin Zinc) Ointment or any topical aminoglycoside in circumstances where significant systemic absorption could occur.

Warnings

General

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.

Following significant systemic absorption: aminoglycosides such as neomycin can cause irreversible ototoxicity; neomycin sulfate, polymyxin B sulfate, and bacitracin zinc have nephrotoxic potential; polymyxin B sulfate has neurotoxic potential.

The concurrent use of other aminoglycoside antibiotics is not recommended in circumstances where significant systemic absorption of neomycin sulfate following topical application could occur.

Gastrointestinal

Clostridium difficile-associated disease:

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *Clostridium difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases.

Precautions

General

The use of NEOSPORIN® should not be continued for more than 7 days without medical supervision. If the infection is not improved after one week, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether therapy should be changed (see Warnings section).

Articles in current medical literature indicate an increase in the incidence of allergies to neomycin in patient with stasis ulcers or eczema. The possibility of an allergic reaction to neomycin should be borne in mind.

As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible.

After a maximal course, treatment should not be repeated for at least 3 months.

Avoid introduction of NEOSPORIN® ointment into the eye. If NEOSPORIN® ointment is accidentally introduced into the eye, the eye should be rinsed thoroughly with cold water.

NEOSPORIN® should be kept out of reach of children.

Use in the Elderly

NEOSPORIN® is suitable for use in elderly patients. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulfate may occur (see Dosage and Administration section).

Use in Children

NEOSPORIN® is suitable for use in children (2 years and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus NEOSPORIN® is not recommended for use in neonates and infants (<2 years) (see Contraindications and Dosage and Administration sections).

Use in Pregnancy

There is little information to demonstrate the possible effect of topically applied neomycin in pregnancy. However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity, thus use of NEOSPORIN® is not recommended in pregnancy.

Nursing Mothers

There is little information to demonstrate the possible effect of topically applied neomycin in lactation. Thus, use of NEOSPORIN® is not recommended in nursing mothers.

Patients with Special Diseases and Conditions

In renal impairment the plasma clearance of neomycin is reduced (see Dosage and Administration).

Drug Interactions

Following significant systemic absorption, both neomycin sulfate and polymyxin B sulfate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents. However, the neuromuscular blocking activity of neomycin sulfate and polymyxin B sulfate is unlikely to present a hazard during use of NEOSPORIN®.

Adverse Reactions

Adverse reactions have occurred with topical use of antibiotic combination containing 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 1 clinical study, using a 20% neomycin patch, neomycin-induced allergic skin reactions occurred in two of 2175 (0.09%) individuals in the general population. In another study the incidence was found to be approximately 1%.

Ototoxicity and nephrotoxicity have been reported (see Warnings section).

Stinging and burning have been reported rarely when this product has gained access to the middle ear.

The incidence of allergic hypersensitivity reactions to neomycin sulphate in the general population are low. There is, however, an increased incidence of hypersensivity to neomycin sulfate in certain selected groups of patients in dermatological practice, particularly those with venous stasis eczema and ulceration, and chronic otitis externa.

Allergic hypersensitivity to neomycin following topical use may manifest itself as an eczematous exacerbation with reddening, scaling, swelling and itching of the affected skin, or as a failure of the lesion to heal.

Allergic hypersensitivity reactions following the topical administration of bacitracin zinc and polymyxin B sulfate are rare events.

Anaphylactic reactions following the topical application of bacitracin zinc have been reported, but are rare events.

Postmarketing Data

Immune System Disorders

Application site hypersensitivity.

General Disorders and Administration Site Conditions

Application site reaction including pain, erythema, edema, pruritus and exacerbation of underlying skin conditions.

Symptoms and Treatment of Overdosage

Symptoms

No specific symptoms or signs have been associated with excessive use of NEOSPORIN®. However, consideration should be given to significant systemic absorption (see Contraindications, Warnings, and Precautions sections).

Following accidental ingestion, minimal absorption is expected.

Treatment

Use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored.

Blood levels of neomycin sulfate, polymyxin B, and bacitracin zinc should be determined. Hemodialysis may reduce the serum level of neomycin sulfate.

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

Dosage and Administration

NEOSPORIN® ointment is for topical skin administration only. Treatment should not be continued for more than 7 days without medical supervision.

Use in Adults

Prior to treatment, remove any debris such as pus, crusts, etc. from the affected area; apply a thin film to the affected area 2 to 5 times per day, depending on the clinical condition. Cover with dressing or leave exposed.

Do not use in the eyes.

Use in Children

NEOSPORIN® is suitable for use in children (2 years and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus NEOSPORIN® is not recommended for use in neonates and infants (<2 years) (see Contraindications and Precautions sections).

Use in the Elderly

NEOSPORIN® is suitable for use in elderly patients. Caution should be exercised in cases where a decrease in renal function exists and significant systemic

absorption of neomycin sulfate may occur (see Warnings, and Precautions sections).

Use in Renal Impairment

Dosage should be reduced in patients with reduced renal function (see Precautions section).

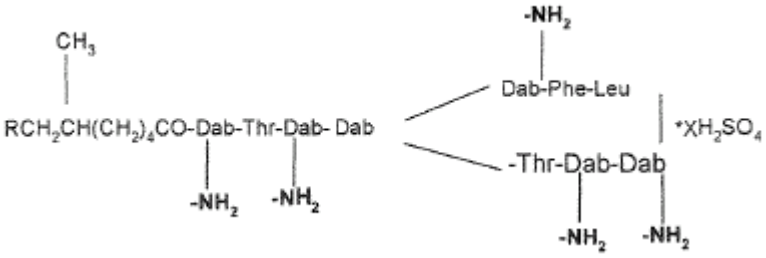
Pharmaceutical Information

Drug Substance

NEOSPORIN® formulations are antibacterial preparations for topical use.

Polymyxin B Sulfate

Polymyxin B sulfate is the sulfate salt of polymyxin B_1 and B_2, 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:



Polymyxin B_1:

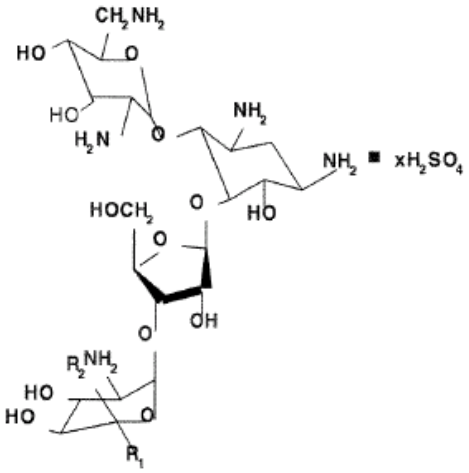
R=CH_3

Polymyxin B_2:

R=H DAB = α,γ-diaminobutyric acid

Neomycin Sulfate

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 600µg of neomycin standard per mg, 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

Composition

Each g contains: polymyxin B sulfate 5,000 units, bacitracin zinc 400 units, and neomycin sulfate 5mg in a low melting point petrolatum base.

Stability and Storage Recommendations

Store NEOSPORIN® Ointment (Neomycin and Polymyxin B Sulfates and Bacitracin Zinc) between 15° to 25°C.

Special Instructions

Dilution of NEOSPORIN® is not recommended; reduction of the antibiotic concentrations may reduce their therapeutic efficacy.

Availability of Dosage Forms

NEOSPORIN® (Neomycin and Polymyxin B Sulfates, and Bacitracin Zinc) Ointment is available in tubes of 15g.

Information for the Consumer

General

If redness, irritation, swelling or pain persists or increases, discontinue use and notify your physician.

References

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3. Forstrom L, Pirila V, Pirila L Cross-sensitivity within the neomycin group of antibiotics. Acta Dermato-Venereologica 1979; 59: 67-69.

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