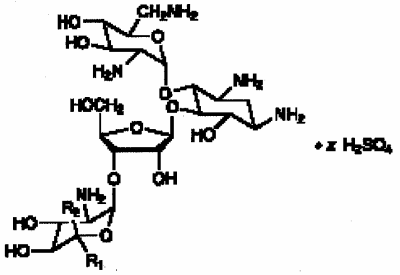
CORTISPORIN® Ointment

(neomycin and polymyxin B sulfates, bacitracin zinc, and hydrocortisone ointment, USP)

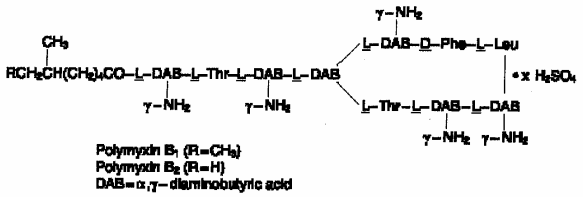
DESCRIPTION: CORTISPORIN Ointment (neomycin and polymyxin B sulfates, bacitracin zinc, and hydrocortisone ointment, USP) is a topical antibacterial ointment. Each gram contains: neomycin sulfate equivalent to 3.5 mg neomycin base, polymyxin B sulfate equivalent to 5,000 polymyxin B units, bacitracin zinc equivalent to 400 bacitracin units, hydrocortisone 10 mg (1%), and white petrolatum, qs.

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 µg of neomycin standard per mg, calculated on an anhydrous basis. The structural formulae are:

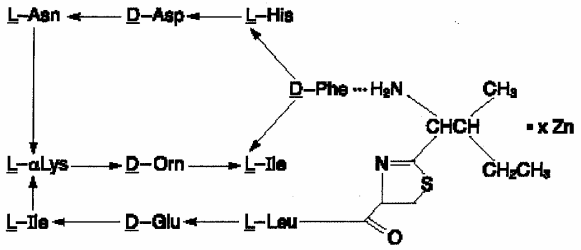


Neomycin B (R_1=H, R_2=CH_2NH_2)
Neomycin C (R_1=CH_2NH_2, R_2=H)

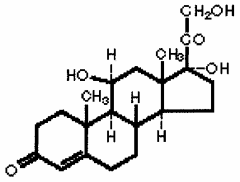
Polymyxin B sulfate is the sulfate salt of polymyxin B_1 and B_2, which are produced by the growth of *Bacillus polymyxa* (Prazmowski) Migula (Fam. Bacillaceae). It has a potency of not less than 6,000 polymyxin B units per mg, calculated on an anhydrous basis. The structural formulae are:



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* (Fam. Bacillaceae). It has a potency of not less than 40 bacitracin units per mg. The structural formula is:



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



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. Polymyxin B sulfate, bacitracin zinc, and neomycin sulfate together are considered active against the following microorganisms: *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*.

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

INDICATIONS AND USAGE: For the treatment of corticosteroid-responsive dermatoses with secondary infection. It has not been demonstrated that this steroid-antibiotic combination provides greater benefit than the steroid component alone after 7 days of treatment. (See **WARNINGS**.)

CONTRAINDICATIONS: Not for use in the eyes or in the external ear canal if the eardrum is perforated. This product is contraindicated in tuberculous, fungal, or viral (for example, herpes simplex or varicella zoster) lesions of the skin. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNINGS: Neomycin can induce permanent sensorineural hearing loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti. The risk of ototoxicity is greater with prolonged use.

Therapy with this product should be limited to 7 days of treatment. (See **INDICATIONS AND USAGE**.)

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

When using neomycin-containing products to control secondary infection in the chronic dermatoses, such as chronic otitis extema 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 manifest 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. Treatment should not be continued for longer than 7 days. 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. Allergic cross-reactions may occur which could prevent the use of any or all of the aminoglycoside antibiotics for the treatment of future infections.

Use of steroids on infected areas should be supervised with care as anti-inflammatory steroids may encourage spread of infections. If this occurs, steroid therapy should be stopped and appropriate antibacterial drugs used. Generalized dermatological conditions may require systemic corticosteroid therapy.

Signs and symptoms of exogenous hyperadrenocorticism can occur with the use of topical corticosteroids, including adrenal suppression. Systemic absorption of topically applied steroids will be increased if extensive body surface areas are treated or if occlusive dressings are used. Under these circumstances, suitable precautions should be taken when long-term use is anticipated.

Information for Patients: If redness, irritation, swelling, or pain persists or increases, discontinue use and notify physician. Do not use in the eyes.

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 CORTISPORIN Ointment is used by a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established. Sufficient percutaneous absorption of hydrocortisone can occur in infants and children during prolonged use to cause cessation of growth, as well as other signs and symptoms of hyperadrenocorticism.

Geriatric Use: Clinical studies of Cortisporin Ointment 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 elderly and younger patients.

In accordance with 21 CFR 201.57(f)(10)(ii)(A)

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, bacitracin, 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.[1] In another study, the incidence was found to be approximately 1%.[2]

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.

When steroid preparations are used for long periods of time in intertriginous areas or over extensive body areas, with or without occlusive non-permeable dressings, striae may occur; also there exists the possibility of systemic side effects when steroid preparations are used over large areas or for a long period of time.

DOSAGE AND ADMINISTRATION: Therapy with this product should be limited to 7 days. A thin film is applied 2 to 4 times daily to the affected area.

HOW SUPPLIED: Tube of 1/2 oz with applicator tip (NDC 61570-031-50).

Store at 15° to 25°C (59° to 77°F).

REFERENCES:

1. Leyden JJ, Kligman AM. Contact dermatitis to neomycin sulfate. *JAMA*. 1979;242:1276-1278.
2. Prystowsky SD, Allen AM, Smith RW, et al. Allergic contact hypersensitivity to nickel, neomycin, ethylenediamine, and benzocaine. *Arch Dermatol*. 1979;115:959-962.

Prescribing Information as of September 2003.

Update
Rev Date

Monarch Pharmaceuticals®

Distributed by: Monarch Pharmaceuticals, Inc., Bristol, TN 37620

(A wholly owned subsidiary of King Pharmaceuticals, Inc.)

Manufactured by: King Pharmaceuticals, Inc., Bristol, TN 37620

~~0934082~~

~~Rev. 4/00~~

Update
Item #