

LOG NO. 1032

NEOSPORIN

OPHTHALMIC

SOLUTION

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

Division of Medical Sciences

1032

DRUG EFFICACY STUDY

Form A

(To be submitted in duplicate by applicant)

1. NDA Number 9-580 60532 2. Date Originally Approved April 11, 1955 3. Rx OTC

4. Brand Name 'Neosporin' brand Polymyxin B-Neomycin-Gramicidin Ophthalmic Solution

5. Applicant's Name Burroughs Wellcome & Co. (U.S.A.) Inc.

and Address 1 Scarsdale Road, Tuckahoe, New York 10707

6. Quantitative Formula

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	Amount (per tablet, per ml., etc.) <u>per ml.</u>
Polymyxin B Sulfate	5,000 units
Neomycin Sulfate	2.5 mg.
	(equivalent to 1.75 mg. Neomycin Base)
Gramicidin	0.025 mg.

7. Dosage Form (tablets, etc.) Solution

8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used.) Topical

9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).

10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).)

11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.

12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white).

Blue copy is original
White copy is duplicate

The back of this form may be used if additional space is needed.

'Neosporin' brand Polymyxin B-Neomycin-Gramicidin Ophthalmic Solution

1. Brownlee, George et al.: The Chemotherapy and Pharmacology of the Polymyxins Brit. J. Pharm. and Chemo. 7:170 (March) 1952
2. Jawetz, Ernest: Polymyxin, Colistin and Bacitracin Ped. Clinics of North America 8:1057 (Nov.) 1961
3. Wiggins, R.L.: Experimental Studies on the Eye with Polymyxin B Amer. J. Ophth. 35:83 (May) 1952
4. Vogel, Adolph W. et al.: Ocular-Tissue Tolerance and Penetration When Locally Applied in the Rabbit Eye Amer. J. Ophth. 34:1357 (1951)
5. Lopez, Severino P.: Topical Use of Neomycin in Ophthalmology Anti. & Chemo. 4:1189 (Dec.) 1954
6. Sorsby, Arnold et al.: Neomycin in Ophthalmology Ann. Roy. Col. Surg. 22:107 (1958)
7. Robinson, Harry J. et al.: In Vitro and In Vivo Studies of Gramicidin, Tyrothricin and Tyrocidine J. Pharm. & Exper. Therap. 76:316 (1942)
8. Lask, S.A.: Tyrothricin as an Antibiotic Arch. Surg. 56:475 (1948)
9. Ainslie, D.: Treatment of Superficial Ocular Infection with a Polymyxin-Bacitracin Ointment (Polyfax) Brit. J. Ophth. 39:557 (1955)
10. Hallett, Joseph W. et al.: Ophthalmic Use of Neosporin Amer. J. Ophth. 41:850 (May) 1956

ISSUE DETACHED

For the Medical Profession only

'NEOSPORIN'[®] brand
POLYMYXIN B-NEOMYCIN-GRAMICIDIN
OPHTHALMIC SOLUTION

STERILE

DESCRIPTION

Each cc. contains:

'Aerosporin' brand Polymyxin B* Sulfate	5,000 Units
Neomycin Sulfate	2.5 mg.
(equivalent to 1.75 mg. Neomycin Base)	
Gramicidin	0.025 mg.

Vehicle contains alcohol 0.5%, thimerosal (preservative) 0.001%, and the inactive ingredients propylene glycol, polyoxyethylene polyoxypropylene compound, sodium chloride and purified water.

'Neosporin' brand Polymyxin B-Neomycin-Gramicidin Ophthalmic Solution is a sterile preparation indicated for the prophylaxis and treatment of bacterial infections of the eye due to susceptible organisms. It is particularly useful in situations in which an ophthalmic solution is preferred to an ointment, as in preoperative and postoperative use in ophthalmic surgery, and in corneal wounds, and when an ointment base might interfere with the visual acuity of ambulatory patients engaged in normal activity.

ACTION

The combination of 'Aerosporin' brand Polymyxin B Sulfate with gramicidin and neomycin is chosen for the completeness of its antibacterial action against most pathogens likely to occur in the eye.

Polymyxin B attacks gram-negative bacilli, including virtually all strains of *Pseudomonas aeruginosa*. This organism is a notable omission from the spectra of most other agents, but it is highly susceptible to polymyxin B which is acknowledged to be the most effective agent known for treatment and prophylaxis of *Pseudomonas* infections. The frequency with which gram-negative bacilli, especially *Ps. aeruginosa* and *H. influenzae* (Koch-Weeks bacillus) invade susceptible mucous membranes of the eye makes polymyxin B indispensable in these fields.

Neomycin provides antibacterial action against many strains of gram-positive and gram-negative organisms, including many strains of *Proteus vulgaris*. Neomycin is considered by many authorities to be one of the most effective antibiotics against *Staphylococcus aureus* which has been demonstrated to be one of the most common etiological organisms in bacterial conjunctivitis.

Gramicidin is active against most gram-positive bacilli and cocci, and

extends the spectrum to include hemolytic streptococci, thus completing the antibacterial scope of the ophthalmic solution.

INDICATIONS

For the treatment of external bacterial infections of the eye, including acute and chronic conjunctivitis, pink eye, infected sockets, corneal ulcers, keratitis, episcleritis, blepharitis, and dacryocystitis. Prophylactically, it is useful following removal of foreign bodies, and before and after ophthalmic surgery, to help provide and maintain a sterile field.

The solution is bland and well tolerated in the eye. The saline vehicle is non-irritant since its tonicity has been adjusted to that of the tears which overlay the cornea. It is entirely suitable for use in infants and children as well as adults. The incidence of sensitivity to the component antibiotics is very low, and bacteria rarely develop resistance to them. If irritation occurs, the use of the solution should be discontinued.

APPLICATION

The suggested dosage is one or two drops in the affected eye, two to four times daily, or more frequently, as required. In acute infections initiate therapy with one or two drops every 15 to 30 minutes, reducing the frequency of instillation gradually as the infection is controlled.

The patient should be instructed to avoid contaminating the eye dropper with material from an infected eye or other source. This is best done by preventing the tip of the eye dropper from touching the eyelid or surrounding areas. This caution is necessary in order to keep the sterile solution as free from contaminating organisms as possible.

CONTRAINDICATIONS

This product is contraindicated for subconjunctival or intraocular injection, or for irrigation of fistulous tracts. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

CAUTION

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

PREPARATION

'NEOSPORIN'[®] brand

POLYMYXIN B-NEOMYCIN-GRAMICIDIN
OPHTHALMIC SOLUTION
STERILE

Bottle of 10 cc. with sterile dropper.

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* U.S. PATENT NOS. 2,565,057 & 2,695,261



BURROUGHS WELLCOME & CO. (U.S.A.) INC.
TUCKAHOE, NEW YORK BURLINGAME, CALIFORNIA

Printed in U.S.A.

May 1964

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NEOSPORIN OPHTHALMIC SOLUTION
NDA ~~9590~~ 60582
LOG 1032

Panel on Drugs Used in Ophthalmology

INDICATIONS

- I. For prophylaxis against ocular infection.

EVALUATION: Possibly effective.

COMMENTS: The Panel feels that there is no adequate support of prophylactic value and feels that nonsusceptible organism growth may be favored.

DOCUMENTATION: None applicable.

- II. For the treatment of virtually all strains of *Pseudomonas aeruginosa*, *H. influenzae* (Koch-Weeks bacillus), many strains *Proteus vulgaris*, *Staphylococcus aureus*, hemolytic streptococci and most gram positive bacilli and cocci.

EVALUATION: Effective.

COMMENTS: None.

DOCUMENTATION:

1. Ainslie, D. Treatment of superficial ocular infection with a polymyxin-bacitracin ointment (polyfax). *Brit. J. Ophthal.* 39:557-562, 1955.
2. Brownlee, G., S.R.M. Bushby, and E.I. Short. The chemotherapy and pharmacology of the polymyxins. *Brit. J. Pharmacol.* 7:170-188, 1952.
3. Hallett, J.W., M.I. Wolkowicz, and I.H. Leopold. Ophthalmic use of neosporin. *Amer. J. Ophthal.* 41:850-853, 1956.
4. Jawetz, E. Polymyxin, colistin and bacitracin. *Pediat. Clin. N. Amer.* 8:1057-1071, 1961.
5. Lask, S.A. Tyrothricin as an antibiotic. *Arch. Surg. (Chicago)* 56:475-483, 1948.
6. Lopez, S.P. Topical use of neomycin in ophthalmology; a preliminary report. *Antibiot. Chemother. (N.Y.)* 4:1189-1195, 1954.
7. Robinson, H.J., and O.E. Graessle. In vitro and in vivo studies of gramicidin, tyrothricin and tyrocidine. *J. Pharmacol. Exp. Ther.* 76:316-325, 1942.
8. Sorsby, A., and J. Ungar. Neomycin in ophthalmology. *Ann. Roy. Coll. Surg. Eng.* 22:107-116, 1958.
9. Vogel, A.W., I.H. Leopold, and A. Nichols. Neomycin; ocular-tissue tolerance and penetration when locally applied in the rabbit eye. *Amer. J. Ophthal.* 34:1357-1362, (October) 1951.
10. Wiggins, R.L. Experimental studies on the eye with polymyxin B. *Amer. J. Ophthal.* 35:83-99, (May, Pt.2) 1952.)

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III. For the treatment of external ocular infections such as acute and chronic conjunctivitis, pink eye, corneal ulcers, keratitis.

EVALUATION: Possibly effective.

COMMENTS: Although the individual components may be effective in the topical treatment of susceptible ocular infections, there is no evidence that their combination provides any increased therapeutic efficacy.

DOCUMENTATION: None applicable.

IV. For the treatment of blepharitis, dacryocystitis, episcleritis.

EVALUATION: Possibly effective.

COMMENTS: The Panel feels that there is no evidence showing adequate penetration or effective therapy of these conditions.

DOCUMENTATION: None applicable.

V. For use before and after ocular surgery to help provide and maintain a sterile field.

EVALUATION: Possibly effective.

COMMENTS: This claim must either be supported or deleted from the insert.

DOCUMENTATION: None applicable.

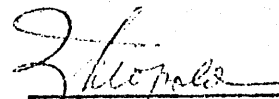
VI. For use prophylactically after removal of foreign bodies.

EVALUATION: Possibly effective.

COMMENTS: The Panel feels that there is no adequate support for prophylactic value and feels that the growth of nonsensitive organisms may be favored.

DOCUMENTATION: None applicable.

Signature



Irving Leopold, M.D., Chairman
Ophthalmology Panel