For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

NEOSPORIN-H ANTIBIOTIC OINTMENT WITH HYDROCORTISONE

For Skin and Ophthalmic Use

1. GENERIC NAME

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

NEOSPORIN-H ANTIBIOTIC OINTMENT WITH HYDROCORTISONE (for skin and ophthalmic use)

Each gram contains:
Polymyxin B Sulphate IP equivalent to Polymyxin B 5000 units
Bacitracin Zinc IP equivalent to Bacitracin 400 units
Neomycin Sulphate IP equivalent to Neomycin 3400 units
Hydrocortisone IP 10 mg

3. DOSAGE FORM AND STRENGTH

Ointment (for topical and ophthalmic use)

NEOSPORIN-H ANTIBIOTIC OINTMENT WITH HYDROCORTISONE (for skin and ophthalmic use)

Each gram contains:
Polymyxin B Sulphate IP equivalent to Polymyxin B 5000 units
Bacitracin Zinc IP equivalent to Bacitracin 400 units
Neomycin Sulphate IP equivalent to Neomycin 3400 units
Hydrocortisone IP 10 mg

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

For skin use

Indicated for the topical treatment of the following conditions:

- eczema/dermatitis including atopic eczema, primary irritant dermatitis, contact allergic dermatitis, seborrhoeic dermatitis and intertriginous conditions in which bacterial infection is present or likely to occur;
- secondarily-infected insect bites.

The use of *NEOSPORIN-H OINTMENT* does not exclude concomitant systemic therapy with other agents (for example antibiotics) where appropriate (see *4.4 Special Warnings and Precautions for Use*).

For ophthalmic use

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 conjunctivitides 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

NEOSPORIN-H OINTMENT can be used for skin and ophthalmic use but the same tube should not be used simultaneously for skin and eye infections i.e. two separate tubes should be used.

4.2. Posology and Method of Administration

Populations

- *Adults*

For skin use

Prior to treatment, remove any debris such as pus, crusts, etc. from the affected area and then apply a thin film of ointment to the affected area one to three times per day, depending on the clinical condition.

Treatment should not be continued for more than seven days without medical supervision.

For ophthalmic use

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

Treatment should not be continued for more than seven days without medical supervision.

- *Children and infants*

NEOSPORIN-H OINTMENT 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 -H OINTMENT* is not recommended for use in neonates and infants (less than 2 years) (*see 4.3 Contraindications* and *4.4 Special Warnings and Precautions for Use*).

- *Elderly*

NEOSPORIN-H OINTMENT is suitable for use in the elderly. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulphate may occur *(see 4.4 Special Warnings and Precautions for Use).*

- *Renal Impairment*

Dosage should be reduced in patients with reduced renal function *(see 4.4 Special Warnings and Precautions for Use).*

4.3. Contraindications

The use of *NEOSPORIN-H OINTMENT* is contraindicated in patients who are hypersensitive to neomycin sulphate, bacitracin zinc, polymyxin B sulphate, hydrocortisone, mineral oils or to cross-sensitising substances. Cross-sensitization between neomycin and framycetin, kanamycin, gentamycin and other related antibiotics does occur.

The presence of pre-existing nerve deafness is a contraindication to the use of *NEOSPORIN-H OINTMENT* in circumstances in which significant systemic absorption could occur.

NEOSPORIN-H OINTMENT should not be used to treat otitis externa in the presence of a perforated tympanic membrane because of the risk of ototoxicity.

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

NEOSPORIN-H 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 (tuberculous) infection of the eye, primary bacterial and fungal diseases of ocular structures.

Viral, tuberculous, primary bacterial and fungal infections of the skin are contraindications to the use of *NEOSPORIN-H OINTMENT*

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

NEOSPORIN H OINTMENT should not be used during surgical procedures or before surgery in circumstances where the product could gain access to intraocular fluids.

4.4. Special Warnings and Precautions for Use

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

All topically active corticosteroids possess the potential to suppress the pituitary-adrenal axis following systemic absorption, which is enhanced by occlusive dressings.

Visual disturbance has been reported by patients using systemic and/or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include central serious chorioretinopathy.

The use of *NEOSPORIN-H OINTMENT* should not be continued for more than seven days in the absence of any clinical improvement.

Hydrocortisone may mask the allergic effects produced by any component of *NEOSPORIN-H OINTMENT*.

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

In renal impairment the plasma clearance of neomycin is reduced (*see 4.2 Posology and Method of Administration – Renal Impairment*).

As with other corticosteroid/antimicrobial preparations, prolonged use may result in the overgrowth of non-susceptible organisms including fungi.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is unlikely to occur with topically applied antibiotics, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Accidental maladministration, prescription and dispensing errors have been reported.
Particular care should be taken to ensure that the correct formulation has been provided and administered.

NEOSPORIN-H OINTMENT should be kept out of reach of children.

NEOSPORIN-H OINTMENT contains paraffin. Instruct patients not to smoke or go near naked flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc) that have been in contact with this product burn more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Ophthalmic use:

NOT FOR INJECTION INTO THE EYE. *NEOSPORIN - H 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 immune response and thus increase the hazard of secondary ocular infections. Various ocular diseases and long-term use of topical corticosteroids have been known to cause corneal and scleral thinning. Use of topical corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation.
Acute purulent infections of the eye may be masked or enhanced by the presence of corticosteroid medication.

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. Intraocular pressure should be checked frequently.

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

Use of the 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; frequent slit lamp microscopy is recommended.

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.

The initial prescription and renewal of the medication order 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.

As fungal infections of the cornea are particularly prone to develop coincidentally with long-term corticosteroid applications, fungal invasion should be suspected in any persistent corneal ulceration where a corticosteroid has been used or is in use. Fungal cultures should be taken when appropriate.

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

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.

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.

If inflammation or pain persists longer than 48 hours or becomes aggravated, the patient should be advised to discontinue use of the medication and consult a physician.

This product is sterile when packaged. To prevent contamination, care should be taken to avoid touching the tip of the tube to eyelids or to any other surface. The use of this tube by more than one person may spread infection.

4.5. Drug Interactions

Following significant systemic absorption, both neomycin sulphate and polymyxin B sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents.

However, the neuromuscular blocking activity of neomycin sulphate and polymyxin B sulphate is unlikely to present a hazard during use of *NEOSPORIN-H OINTMENT*.

4.6. Use in Special Populations

- *Children and infants*

NEOSPORIN-H OINTMENT 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 H OINTMENT* is not recommended for use in neonates and infants (less than 2 years) (*see 4.3 Contraindications* and *4.4. Special Warnings and Precautions for Use*).

- *Elderly*

NEOSPORIN-H OINTMENT is suitable for use in the elderly. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulphate may occur *(see 4.4 Special Warnings and Precautions for Use).*

- *Renal Impairment*

Dosage should be reduced in patients with reduced renal function *(see 4.4 Special Warnings and Precautions for Use)*

Pregnancy and Lactation

There is little information to demonstrate the possible effect of topically applied neomycin in pregnancy and lactation. 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-H OINTMENT* is not recommended in pregnancy and lactation.

4.7. Effects on Ability to Drive and Use Machines

Not relevant.

4.8. Undesirable Effects

Skin Use:

The incidence of allergic contact hypersensitivity to neomycin sulphate in the general population is low. There is, however, an increased incidence of hypersensitivity to neomycin in certain selected groups of patients in dermatological practice, in particular venous stasis eczema and ulceration.

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

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

Topically applied hydrocortisone may produce skin atrophy such as telangiectasiae and striae. However, this effect only occurs following prolonged use, high dosage, occlusion of the topical site (for example by plastic or by natural occlusion as in the groin), and particularly applies to infants and young children.

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

Post-marketing Data

Immune System Disorders

Rare: Application site hypersensitivity

General Disorders and Administration Site Conditions

Rare: Headache, application site reaction including pain, erythema, irritation, oedema, burning sensation

Skin and Subcutaneous Tissue Disorders:

Rare: Exfoliative dermatitis, skin atrophy, telangiectasia, striae, exacerbation of underlying skin conditions including eczema.

Ophthalmic Use:

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. 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 the secondary ocular 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 been reported.

If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

Post marketing Data

Eye disorders

Rare: Eye pain, eyelid oedema.

4.9. Overdose

Symptoms and Signs

No information is available concerning accidental ingestion of *NEOSPORIN-H OINTMENT*.

No specific symptoms or signs have been associated with excessive use of *NEOSPORIN-H OINTMENT*. However, consideration should be given to significant systemic absorption *(see 4.4 Special Warnings and Precautions for Use).*

Following accidental ingestion of *NEOSPORIN-H OINTMENT*, 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 sulphate, polymyxin B sulphate and bacitracin zinc should also be determined, and haemodialysis may reduce the serum level of neomycin sulphate.

5. PHARMACOLOGICAL PROPERTIES

5.1. Mechanism of action

Polymyxin B sulphate: Polymyxin B is thought to damage the bacterial cytoplasmic membrane, which subsequently causes leakage of the intracellular components. The drug interferes with the structure and function of outer and cytoplasmic membranes in gram-negative bacteria. The polymyxins interact with lipopolysaccharides and phospholipids of the outer membrane. They

also interact electrostatically by displacing calcium and magnesium from negatively charged phosphate groups of membrane lipids.

Neomycin sulphate: Neomycin is an aminoglycoside antibiotic which acts by binding to a specific protein on the 30S subunit of the microbial ribosome, leading to faulty alignment or recognition with respect to messenger RNA and probably t-RNA during initiation of microbial peptide chain formation. The messenger RNA is misread on the recognition region of the ribosome, resulting in the wrong amino acid being inserted into the peptide. The affected ribosomes are released and may be able to re-initiate and repeat the process, leading to increased proportions of nonfunctional peptide chains.

Bacitracin Zinc: Bacitracin is a mixture of polypeptides derived from Bacillus subtilis. It inhibits growth of bacteria primarily by preventing the formation of peptidoglycan chains needed for cell wall synthesis and by altering membrane permeability.

Hydrocortisone possesses anti-inflammatory, anti-allergic and anti-pruritic activity.

5.2. Pharmacodynamic Properties

Bacitracin zinc, neomycin sulphate and polymyxin B sulphate are all bactericidal antibiotics. Hydrocortisone possesses anti-inflammatory, anti-allergic and anti-pruritic activity.

Skin use:

NEOSPORIN-H OINTMENT is active *in vitro* against a wide range of bacterial pathogens found in superficial dermatological infections. Susceptible organisms include:

Gram-positive:
- *Staphylococcus* spp**.** including *Staphylococcus aureus*
- *Streptococcus* spp**.** including *Streptococcus pyogenes.*

Gram-negative:
- *Enterobacter* spp**.**
- *Escherichia* spp**.**
- *Haemophilus* spp**.**
- *Klebsiella* spp**.**
- *Neisseria* spp**.**
- *Proteus* spp**.**
- *Pseudomonas* spp**.** including *Pseudomonas aeruginosa*.

Ophthalmic Use :

NEOSPORIN-H OINTMENT is a bactericidal preparation, active *in vitro* against the majority of bacterial pathogens associated with ocular infections. The range of activity includes:

Gram-positive:
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Streptococcus pneumoniae (pneumococcus)*
- *Streptococcus pyogenes*

- *Enterococcus faecalis*
- *Viridans streptococcus*

Gram-negative:-
- *Enterobacter* spp
- *Escherichia coli*
- *Haemophilus* spp
- *Klebsiella* spp
- *Neisseria* spp
- *Pseudomonas* spp., including *Pseudomonas aeruginosa*
- *Proteus* spp.

5.3. Pharmacokinetic Properties

Bacitracin zinc, neomycin sulphate and polymyxin B sulphate are not absorbed systemically in significant amounts through intact skin but the possibility of significant absorption exists when extensive raw areas are being treated. Hydrocortisone is partially absorbed through intact skin and this absorption is enhanced when the skin is broken or occluded.

6. NONCLINICAL PROPERTIES

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 concentrations (80 µg/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.

7. DESCRIPTION

NEOSPORIN-H ANTIBIOTIC OINTMENT WITH HYDROCORTISONE (for skin and ophthalmic use)

Each gram contains:
Polymyxin B Sulphate IP equivalent to Polymyxin B 5000 units
Bacitracin Zinc IP equivalent to Bacitracin 400 units
Neomycin Sulphate IP equivalent to Neomycin 3400 units
Hydrocortisone IP 10 mg

List of Excipients

White Soft Paraffin.

8. PHARMACEUTICAL PARTICULARS

8.1. Incompatibilities

No incompatibilities have been identified.

8.2. Shelf-Life

The expiry date is indicated on the label and packaging.

Ophthalmic Use:

Discard within ONE MONTH of opening the tube.

8.3. Packaging Information

Tube in a Carton.

8.4. Storage and Handling Information

Store at temperature not exceeding 30°C. Do not freeze.

Dilution of *NEOSPORIN-H OINTMENT* is not recommended; reduction of the antibiotic concentration may reduce their therapeutic efficacy.

Use separate tubes for eye and skin infections.

Sterile until opened. Use within one month after opening the tube.

If irritation persists or increases when the ointment is used in the eye, discontinue its use and consult a physician.

Keep out of reach of children.

FOR EXTERNAL USE ONLY.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or their patient's caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *NEOSPORIN-H OINTMENT*. Patients (and/or their patient's caregiver as applicable) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office
Dr. Annie Besant Road, Worli,
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Manufacturing License Number is indicated on the label and packaging.

DATE OF REVISION

15-NOV-2022

Trade marks are owned by or licensed to the GSK group of companies.

Version: NEO-HO/PI/IN/2022/01

Adapted from:

- *Neomycin-polymyxin B- bacitracin hydrocortisone topical ointment GDS Version 11 dated 26 March 2020*
- *Neomycin-polymyxin B- bacitracin topical and opthalmic ointment GDS Version 11 26 March 2020*
- *Cortisporin Ophthalmic Ointment Sterile (neomycin and polymyxin B sulfates, bacitracin zinc, and hydrocortisone ophthalmic ointment, USP) USPI dated 22 March 2004.*