Med Choice Vision Care

# Dexamethasone Neomycin (as sulfate) Polymyxin-B-Sulfate

℞

Maxidin®

**1** mg/**3.5** mg/**6000** I.U.

Ophthalmic and Otic Suspension

CORTICOSTEROID/ANTI-INFECTIVE

**FOR EXTERNAL USE ONLY**

## FORMULATION:

Each mL contains:

Dexamethasone ……..…..…..…….. 1 mg

Neomycin (as sulfate) ……..…..…… 3.5 mg

Polymyxin-B-Sulfate ……..…..…… 6000 I.U.

## PHARMACEUTICAL FORM:

Ophthalmic/Otic Suspension. White sterile suspension for topical use only.

## INDICATIONS:

Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) is indicated for the short-term treatment of steroid responsive conditions of the eye when prophylactic antibiotic treatment is also required, after excluding the presence of fungal and viral disease. Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) is indicated for infections of the external ear canal caused by susceptible organisms; mastoidectomy cavity infections or chronic suppurative otitis media.

## DOSAGE AND ADMINISTRATION:

Children and Adults (including the Elderly):

Eye: Apply 1-2 drops to each affected eye up to 6 times daily or, more frequently if required.

Ear: In external ear canal infection: Before administration, the external ear should be thoroughly cleaned. Apply 4 drops 3-4 times daily.

Topical to Mastoidectomy cavity or Ear canal: Apply 4-10 drops 3-4 times daily.

## CONTRAINDICATIONS:

- Hypersensitivity to the active substances or to any component of the preparation.
- Epithelial Herpes Simplex keratitis.
- Vaccinia, varicella, or other viral infection of cornea and conjunctiva (except Herpes Zoster keratitis).
- Fungal diseases of ocular structures.
- Mycobacterial ocular infections.

## SPECIAL WARNINGS AND PRECAUTIONS:

For topical use only. Not for injection or ingestion. As with all antibacterial preparations, prolonged use may lead to overgrowth of nonsusceptible bacterial strains or fungi. If superinfection occurs, appropriate therapy should be initiated. Sensitivity to topically-applied aminoglycosides may occur in some patients.

Cross-sensitivity to other aminoglycosides may also occur. If signs of serious reactions or hypersensitivity occur, discontinue use of Dexamethasone + Neomycin (as Sulfate) + Polymyxin-B-Sulfate (Maxidin®). Patients using ophthalmic preparations containing neomycin sulphate should be advised to consult a physician if ocular pain, redness, swelling, or irritation worsens or persists. Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic neomycin or when applied topically to open wounds or damaged skin. Nephrotoxic and neurotoxic reactions have also occurred with systemic polymyxin B. Although these effects have not been reported following topical ocular use of this product, caution is advised when used concomitantly with systemic aminoglycoside or polymyxin B therapy. Prolonged use of ophthalmic steroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, reduced visual acuity and visual field defects, and posterior subcapsular cataract formation. In patients receiving prolonged ophthalmic corticosteroid therapy, intraocular pressure should be checked routinely and frequently. This is especially important in pediatric patients, as the risk of corticosteroid induced ocular hypertension may be greater in children and may occur earlier than in adults. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids. Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral, or fungal infections and mask the clinical signs of infection, preventing recognition of ineffectiveness of the antibiotic, or may suppress hypersensitivity reactions to substances in the product. Fungal infection should be suspected in patients with persistent corneal ulceration who have been or are receiving these drugs and corticosteroid therapy should be discontinued if fungal infection occurs. To avoid the risk of enhancement of herpetic corneal disease, frequent slit lamp examination is essential. Contact lens wear is not recommended during treatment of an ocular infection. Therefore patients should be advised not to wear contact lenses during treatment with Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®). Dexamethasone + Neomycin ( as sulfate) + Polymyxin-B-Sulfate (Maxidin®) ophthalmic suspension contains benzalkonium chloride as a preservative which may cause eye irritation and is known to discolor soft contact lenses. Avoid contact with soft contact lenses. Remove contact lenses prior to application and wait at least 15 minutes before reinsertion.

## DRUG INTERACTIONS:

No interaction studies have been performed. Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems.

Concomitant and/or sequential use of an aminoglycoside (neomycin) and other systemic, oral, or topical drugs that have neurotoxic, ototoxic, or nephrotoxic effects may result in additive toxicity and should be avoided, whenever possible. If more than one ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart.

## PREGNANCY AND LACTATION:

**Pregnancy**

There are no or limited amount of data from the use of Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) in pregnant women.

Studies in animals with some active components of Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) have shown reproductive toxicity. Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) is not recommended during pregnancy.

**Lactation**

It is unknown whether topical ophthalmic dexamethasone, neomycin or polymyxin B are excreted in human milk. Because systemic corticosteroids and aminoglycosides may be distributed into milk, a risk to the suckling child cannot be excluded.

A decision must be made whether to discontinue breastfeeding or to discontinue therapy with Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) taking into account the benefit of breastfeeding for the child and the benefit of the product to the woman.

Effects on ability to drive and use machines Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) has no or negligible influence on the ability to drive and use machines. As with any other eye drop, temporarily blurred vision or other visual disturbances may affect the ability to drive or use machines. If transient blurred vision occurs upon instillation, the patient must wait until the vision clears before driving or using machinery.

## ADVERSE DRUG REACTIONS:

The following adverse effects are classified according to the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1000), very rare (< 1/10,000) or not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Immune system disorders: Not known: hypersensitivity (systemic or ocular). Nervous system disorders: Not known: headache.

**Eye disorders:** Uncommon: keratitis, increased intraocular pressure, eye irritation, eye pruritus, ocular discomfort.

**Not known:** corneal thinning, photophobia, blurred vision, mydriasis, eye pain, eye swelling, ptosis, foreign body sensation in eyes, increased lacrimation, ocular hyperaemia.

Description of selected adverse events: Due to the steroid component, in diseases causing thinning of the cornea or sclera there is a higher risk for perforation especially after long treatments.

Topical ophthalmic steroid use may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects. Also it may lead to posterior subcapsular cataract formation.

Sensitivity to topically-administered aminoglycosides may occur in some patients. Systemic side effects may occur with extensive use.

## OVERDOSE AND TREATMENT:

No case of overdose has been reported.

Signs and symptoms of an overdosage of Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) may be similar to adverse reaction effects seen in some patients (punctuate keratitis, erythema, increased lacrimation, edema and lid itching).

A topical ophthalmic overdose of Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) may be flushed from the eye(s) with lukewarm water.

## PHARMACOLOGICAL PROPERTIES:

Pharmacotherapeutic group: ophthalmological & otological preparations; antiinfectives.

## PHARMACODYNAMIC PROPERTIES:

**Mechanism of Action:**

Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) has a dual effect: suppression of inflammation symptoms by the corticosteroidal component dexamethasone, and an anti-infective effect due to the presence of two antibiotics, polymyxin B and neomycin.

Dexamethasone is a synthetic glucocorticoid with potent anti-inflammatory activity. Polymyxin B is a cyclic lipopeptide that penetrates the cell wall of gram-negative bacilli to destabilize the cytoplasmic membrane. It is generally less active against gram-positive bacteria. Neomycin is an aminoglycoside antibiotic that primarily exerts its effect on bacterial cells by inhibiting polypeptide assembly and synthesis on the ribosome.

**Mechanism of Resistance:**

Resistance of bacteria to polymyxin B is of chromosomal origin and is uncommon. A modification of the phospholipids of the cytoplasmic membrane appears to play a role.

Resistance to neomycin occurs by several different mechanisms including (1) alterations of the ribosomal subunit within the bacterial cell; (2) interference with the transport of neomycin into the cell , and (3) inactivation by an array of adenylating, phosphorylating, and acetylating enzymes.

Genetic information for production of inactivating enzymes may be carried on the bacterial chromosome or on plasmids.

**Breakpoints:**

Each mL of Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®) contains 6000 IU Polymyxin B sulfate and 3.5 mg Neomycin. The breakpoints and the *in-vitro* spectrum as mentioned below are based on the dual activity of either Polymyxin B or Neomycin. The breakpoints listed here are based upon acquired resistance for specific species found in ocular infections and the ratio in International Units of Polymyxin B to Neomycin in Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®): Resistance breakpoints: > 5:2.5 to > 40:20 depending upon the bacterial species.

**Susceptibility:**

The information listed below provides guidance on the approximate probabilities on the susceptibility of microorganisms to Polymyxin B or neomycin in Dexamethasone + Neomycin (as sulfate) + Polymyxin-B-Sulfate (Maxidin®). The presentation below lists bacterial species recovered from external ocular infections of the eye.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the combination of Polymyxin B or Neomycin as in Dexamethasone + Neomycin (as sulfate) + Polymyxin-B Sulfate (Maxidin®) in at least some types of infections is questionable.

## COMMONLY SUSCEPTIBLE SPECIES:

**Aerobic Gram-positive microorganisms:**

*Bacillus cereus, Bacillus megaterium, Bacillus pumilus, Bacillus simplex, Corynebacterium accolens, Corynebacterium bovis Corynebacterium macginleyi, Corynebacterium propinquum, Corynebacterium pseudodiphtheriticum, Staphylococcus aureus (methicillin susceptible - MSSA), Staphylococcus capitis, Staphylococcus epidermidis (methicillin susceptible - MSSE), Staphylococcus pasteuri, Staphylococcus warneri, Streptococcus mutans.*

**Aerobic Gram-negative microorganisms:**

*Haemophilus influenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Moraxella lacunata, Pseudomonas aeruginosa, Serratia species.*

## SPECIES FOR WHICH ACQUIRED RESISTANCE MIGHT BE A PROBLEM:

*Staphylococcus epidermidis (methicillin resistant - MRSE), Staphylococcus hominis, Staphylococcus lugdunensis.*

## INHERENTLY RESISTANT ORGANISMS:

**Aerobic Gram-positive microorganisms:**

*Enterococci faecalis, Staphylococcus aureus (methicillin resistant - MRSA), Streptococcus mitis, Streptococcus pneumoniae.*

**Anaerobic Bacteria:**

*Propionibacterium acnes.*

Dexamethasone is a moderately powerful corticosteroid having good penetration in ocular tissue. Corticosteroids have an anti-inflammatory as well as a vasoconstrictive effect.

They suppress the inflammatory response and symptoms in various disorders without basically curing these disorders.

## PHARMACOKINETIC PROPERTIES:

Dexamethasone, like other corticosteroids, is absorbed rapidly after oral administration and has a biological half-life of about 190 minutes. Sufficient absorption may occur after topical application to the skin and eye to produce systemic effects. Intraocular penetration of dexamethasone occurs in significant amounts and contributes to the effectiveness of dexamethasone in anterior segment inflammatory disease.

Polymyxin B sulfate is not absorbed from the gastrointestinal tract or through intact skin, although the intact corneal epithelium prevents penetration into the corneal stroma, therapeutic concentrations do enter the stroma after epithelial damage. Good stromal penetration occurs after epithelial abrasion following topical instillation, subconjunctival injection, or corneal bath. No significant polymyxin B penetration into the vitreous is demonstrable after parenteral or local administration of the drug.

Neomycin is poorly absorbed from the gastrointestinal tract and after topical administration an insufficient amount is absorbed to produce systemic effects.

Absorption has been reported to occur from wounds and inflamed skin. After absorption neomycin is rapidly excreted by the kidneys in active form.

## CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

***"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction."***

## STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

Keep out of reach of children.

## AVAILABILITY:

Box of 1 LDPE Plastic Bottle x 5 mL with HDPE Tamper Proof Cap.

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