SAFETY DATA SHEET

Polymyxin B Sulfate & Trimethoprim Ophthalmic Solution USP

1. PRODUCT AND COMPANY IDENTIFICATION

Product Name: Polymyxin B Sulfate & Trimethoprim Ophthalmic Solution USP
NDC No. 70069-311-01 (10 ml)

Legal Category:

Drug Composition: Antimicrobial\Antibiotic combination

Manufacturer for: Somerset Therapeutics LLC
Customer care: 1-800-417-9175

2. COMPOSITION/INFORMATION ON INGREDIENTS

Description	CAS #
Polymyxin B sulfate	1405-20-5
Trimethoprim sulfate	738-70-5
Benzalkonium chloride	63449-41-2
Sodium chloride	7647-14-5
Sulfuric acid	7664-93-9
Sodium hydroxide	1310-73-2
water for injection	7732-18-5

3. HAZARDS IDENTIFICATION

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EMERGENCY OVERVIEW

Plastic bottle in a cardboard box. Clear, colorless aqueous solution.

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POTENTIAL HEALTH HAZARDS

Carcinogenicity: **(NTP)** No **(IARC)** No **(OSHA)** No

Eye: When used topically Polymyxin B Sulfate is rarely irritating and absorption from the intact skin or mucous membrane is insignificant. Can also cause local irritation on installation and hypersensitivity (anaphylactic) in some individuals. The most frequent adverse reactions are localized irritation consisting of transient burning or stinging or increased redness on installation. Trimethoprim Sulfate and Polymyxin B Sulfate has a low incidence of hypersensitivity (less than 2 of 100 patients) consisting of lid edema, itching, increased redness of the eye (conjunctival erythema), tearing (lacrimation) and/or a rash around the eye (circumocular rash). Although sensitivity reactions are rare, an isolated incident of photosensitivity was reported in a patient who received the drug orally.

Skin: May cause hypersensitivity in some individuals. Possible hypersensitivity responses include rash, pruritus (itching) and exfoliative dermatitis (sheading skin). Although sensitivity reactions are rare, an isolated incident of photosensitivity was reported in a patient who received the drug orally.

Ingestion: May cause irritation and hypersensitivity in some individuals. Ingestion of very large quantities can induce gastric disturbances including nausea, vomiting, headaches, dizziness.

Inhalation: May cause irritation and hypersensitivity in some individuals.

Chronic Effects: May cause irritation and hypersensitivity. As with other antibiotic preparations, prolonged use may result in the overgrowth of non-susceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

Target Organs: Eyes, skin and digestive tract.

Medical Conditions Aggravated by Long Term Exposure:

- Hypersensitivity to antibiotics or any of the component of the product.
- Impairment of fertility: Polymyxin B Sulfate has been reported to impair the motility of

equine sperm, but its effects on male or female fertility are unknown. No adverse effects on fertility or general reproductive performance were observed in rats given trimethoprim in oral doses as high as 70 mg/kg/day for males and 14 mg/kg/day for females.

- Pregnancy:Teratogenic effects: Pregnancy Category C. Animal reproduction studies have not been conducted with Polymyxin B Sulfate. It is not known whether polymyxin B sulfate can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Teratogenic tests of trimethoprim in rats show 40 times the human dose can cause birth defects. Fetal loss (dead and resorbed and malformed fetuses) were shown in rabbits given six times the human dose. Trimethoprim may inhibit folic acid metabolism and should only be used during pregnancy if the potential benefit outweighs the risk to the fetus.

While there are no large well-controlled studies of the use of trimethoprim in pregnant women, Brumfitt and Pursell, in a retrospective study reported the outcome of 186 pregnancies during which the mother received either a placebo or oral trimethoprim in combination with sulfamethoxazole. The incidence of congenital abnormalities was 4.5% (3 of 66) in those who received placebo and 3.3% (4 of 120) in those receiving trimethoprim and sulfamethoxazole. There were no abnormalities in the 10 children whose mothers received the drug during the first trimester. In a separate survey, Brumfitt and Pursell also found no congenital abnormalities in 35 children whose mothers had received oral trimethoprim and sulfamethoxazole at the time of conception or shortly thereafter.

The oral administration of trimethoprim to rats at a dose of 70 mg/kg/day commencing with the last third of gestation and continuing through parturition and lactation caused no deleterious effects on gestation or pup growth and survival.

4. FIRST AID MEASURES

Eyes: If not prescribed this medication, rinse immediately with copious amounts of water for at least 20 minutes. Contact a physician.

Skin: Remove all contaminated clothing and wash skin with copious amounts of water for at least 20 minutes. Contact physician if skin becomes irritated.

Ingestion: Wash out mouth and give plenty of water and bland fluids. Seek professional assistance.

Inhalation: Remove person to fresh air, and if breathing stops, use artificial respiration. Contact physician immediately.

Note to Physicians: None.

5. FIRE FIGHTING MEASURES

Flammable Properties: Flash point: NE Method: NE

Hazardous Products: Emits SO_x, NO_x and toxic fumes.

Extinguishing Media: Dry chemical, carbon dioxide, halon, water spray or fog, and foam on surrounding materials.

Fire Fighting Instructions: Wear self-contained breathing apparatus and protective clothing. Use water spray to keep fire-exposed containers cool. Do not spray water into the burning material.

6. ACCIDENTAL RELEASE MEASURES

Large/Small Spills: Use personal protective equipment. Contain the spill to prevent drainage into sewers, drains or streams. Use absorbent material to solidify the spill. Shovel or scoop up solidified waste. Dispose of material according to Federal, State and Local regulations.

7. HANDLING AND STORAGE

Handling: Avoid contact with product and use caution to prevent puncturing containers. No special protective equipment or procedures are required in the clinical or home environment.

Storage: Store product upright in original containers with the cap tightly closed at a controlled room temperature 15^0-30^0 C (59^0- 86^0 F). **KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.**

8. EXPOSURE CONTROL/PERSONAL PROTECTION

Engineering Controls: In the manufacturing plant, provide adequate ventilation for the raw material handling and compounding process which will maintain the dust and vapor levels below the TLV, STEL, and PEL values for the ingredients. Ventilation fans should be explosion proof. Use adequate personal protective equipment e.g. NIOSH-approved respirators, goggles or safety glasses, gloves and protective clothing. Ensure training in the handling of chemical material and use current Material Safety Data Sheets.

Eye Protection: (29 CFR 1910.133) Recommend goggles or chemical safety glasses.

Skin Protection: Thick impermeable gloves and protective clothing.

Respiratory Protection: (29 CFR 1910.134) NIOSH approved respirator, with organic vapor, acid gas and HEPA filter recommended for handling raw materials. **Warning: Do not use air purifying respirators in oxygen depleted environments**. No respiratory protection is required in the clinical or home environment.

Other: None

Ventilation: Recommended

Contaminated Equipment: Wash contaminated clothing separately. Wash equipment with soap and water. Release rinse water into an approved wastewater system or according to Federal, State and Local regulations.

9. CHEMICAL & PHYSICAL PROPERTIES

Polymyxin B Sulfate:

Description : A White or almost white powder.
Solubility : Polymyxin B sulfate is soluble in water, slightly soluble in alcohol.
Physical state : Polymyxin B sulfate as manufactured by Xellia is a lyophilised powder.
pH in aqueous solutions : 0.5 % solution in water has pH 5.0-7.5 (USP) and 2% solution has 5.0-7.0 (

Trimethoprim:

Description : White to cream colored crystals or crystalline powder.
Solubility : Soluble in benzyl alcohol; sparingly soluble in chloroform and in methanol; slightly soluble in alcohol and in acetone; very slightly soluble in water; practically insoluble in ether and in carbon tetrachloride.
Melting point : 199°C to 203°C
Loss on drying : Not more than 0.5%
Optical Rotation: Trimethoprim exhibits no optical activity.

10. STABILITY AND REACTIVITY

Chemical Stability: Stable

Conditions to avoid: Extreme heat or cold.

Incompatibility: Strong oxidizers and flame.

Hazardous Decomposition Products: Emits SO_X, NO_X and toxic fumes.

Hazardous Polymerization: Should not occur.

11. TOXICOLOGY INFORMATION

Summary of Risks: Toxicological information refers to raw materials product. Concentrations and toxicological effects are substantially reduced in the product. For more detailed information see MSDS on chemical material.

CAS #

1404-26-8 **Polymyxin B Sulfate**

May cause irritation to skin, mucous membranes and respiratory tract. Prolonged and repeated contact can produce hypersensitivity (anaphylactic) in some individuals. Overexposure may produce dizziness, diminished muscular coordination, kidney damage (nephrotoxicity), and sensory disturbances. This material is not readily absorbed into the gut and does not present a toxicological hazard. IV- mouse LD_{50} 5.4 mg/kg, IP- mouse 20.5 mg/kg, Oral- mouse 790 mg/kg,SC- mouse LD_{50} 59.5 mg/kg.

738-70-5 **Trimethoprim**

May cause irritation to the mucous membranes of the eyes, skin, digestive and respiratory tract. Overexposure symptoms due to ingestion of more than one gram include nausea, vomiting, headaches, confusion, mental depression, dizziness, and bone marrow depression. Possible hypersensitivity responses include rash, pruritus (itching), exfoliative dermatitis (sheading skin). Teratogenic tests in rats show 40 times the human dose can cause birth defects. Fetal loss (dead and resorbed and malformed fetuses) were shown in rabbits given six times the human dose. Trimethoprim may inhibit folic acid metabolism and should only be used during pregnancy if the potential benefit outweighs the risk to the fetus. Oral-rat LD_{50} 200 mg/Kg, Intraperitoneal-rat LD_{50} 1460 mg/Kg, Oral-mouse LD_{50} 3960 mg/Kg, Intraperitoneal-mouse LD_{50} 3500 mg/Kg.

12. ECOLOGICAL INFORMATION

Chemical Fate Information: Product administered to patients presents a negligible impact on the environment.

13. DISPOSAL INFORMATION

Dispose of material according to Federal, State, and Local regulations. Themethod typically used is incineration.

EPA Designations: RCRA Hazardous Waste: Not Listed

SARA Title III: Not Listed

14. TRANSPORTATION INFORMATION

Transportation Data: Not classified as hazardous by DOT regulations.

15. REGULATORY INFORMATION

DOT Designations: Not classified as hazardous by DOT regulations.

EPA Designations: RCRA Hazardous Waste
(40 CFR 261.33) Not Listed

FDA Designations: Prescription only medication.
NDC No. 24208-315-10 (10 ml)

OSHA Designations: (29 CFR 1910.1000, Table Z)
Not Listed

SARA Title III: Not listed under Section 313 of Toxic Release Reporting.

CALIFORNIA PROPOSITION 65: Not Listed

16. OTHER INFORMATION

None

The information contained herein is furnished without warranty of any kind. The above information is believed to be correct but does not purport to be all-inclusive and should be used only as a guide. Users should make independent determinations of the suitability and completeness of information from all sources to assure proper use and disposal of these materials and the safety and health of employees and customers.

NE- Not Established
< - Less Than
> - Greater Than

END OF MATERIAL SAFETY DATA SHEET