SAFETY DATA SHEET

Revision Date 13-Jul-2016 **Version** 1

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

Product identifier
Product Name POLYTRIM (polymyxin B sulfate and trimethoprim ophthalmic solution, USP)

Other means of identification
Product Code FP-64
Synonyms Polymyxin B Sulfate and Trimethoprim

Recommended use of the chemical and restrictions on use
Recommended Use Antibiotic

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.

Details of the supplier of the safety data sheet
Manufacturer
ALLERGAN
400 Interpace Parkway, Morris Corporate Center III
Parsippany, NJ 07054, USA
+1-800-272-5525
E-mail address SDS@Actavis.com

Emergency telephone number
Emergency Telephone Call CHEMTREC Day or Night
Within USA or Canada: 1-800-424-9300
Outside USA and Canada: +1-703-741-5970 (collect calls accepted)

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status
This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Reproductive toxicity	Category 2
Effects on or via lactation	Yes

Label elements

Emergency Overview

Warning

Hazard statements
H361 - Suspected of damaging fertility or the unborn child
H362 - May cause harm to breast-fed children

Appearance Liquid **Physical state** Liquid **Odor** No information available

Chemical Name	Symptoms
Polymyxin B Sulfate	The most frequent adverse reaction to this Ophthalmic Solution is local irritation consisting of increased redness, burning, stinging, and/or itching. This may occur on instillation, within 48 hours, or at any time with extended use. There are also multiple reports of hypersensitivity reactions consisting of lid edema, itching, increased redness, tearing, and/or circumocular rash. Photosensitivity has been reported in patients taking oral trimethoprim. Albuminuria, cylinduria, azotemia, and rising blood levels without any increase in dosage.Neurotoxic reactions: Facial flushing, dizziness progressing to ataxia, drowsiness, peripheral paresthesias (circumoral and stocking glove), apnea due to concurrent use of curariform muscle relaxants, other neurotoxic drugs or inadvertent overdosage, and signs of meningeal irritation with intrathecal administration, e.g., fever, headache, stiff neck and increased cell count and protein cerebrospinal fluid.
Trimethoprim	The adverse effects encountered most often with trimethoprim were rash and pruritus. Rare reports of exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell Syndrome), and anaphylaxis have been received. Epigastric distress, nausea, vomiting, and glossitis. Elevation of serum transaminase and bilirubin has been noted, but the significance of this finding is unknown. Cholestatic jaundice has been rarely reported. Thrombocytopenia, leukopenia, neutropenia, megaloblastic anemia, and methemoglobinemia, Hyperkalemia, hyponatremia, aseptic meningitis has been rarely reported. Fever and increases in BUN and serum creatinine levels.

Chemical Name	Medical Conditions Aggravated by Exposure
Polymyxin B Sulfate	Known hypersensitivity to this medication Avoid concurrent use of a curariform muscle relaxant and other neurotoxic drugs (ether, tubocurarine, succinylcholine, gallamine, decamethonium and sodium citrate) which may precipitate respiratory depression
Trimethoprim	This medication is contraindicated in individuals hypersensitive to trimethoprim and in those with documented megaloblastic anemia due to folate deficiency.

Precautionary statements
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P405 - Store locked up
P501 - Dispose of contents/ container to an approved waste disposal plant
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P201 - Obtain special instructions before use
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P263 - Avoid contact during pregnancy/while nursing
P264 - Wash face, hands and any exposed skin thoroughly after handling
P270 - Do not eat, drink or smoke when using this product
P308 + P313 - IF exposed or concerned: Get medical advice/attention

Other Information
Unknown Acute Toxicity 1.58% of the mixture consists of ingredient(s) of unknown toxicity

Over the counter drugs in their solid form are considered exempt under the criteria of the Federal OSHA Hazard Communication Standard 20 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limit may be surpassed, than can be considered hazardous

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS No.	EINECS	Weight-%
SODIUM CHLORIDE USP	7647-14-5	231-598-3	30 - 60*
Water	7732-18-5	231-791-2	10 - 30*
Polymyxin B Sulfate	1405-20-5	215-774-7	5 - 10*
Trimethoprim	738-70-5	212-006-2	3 - 7*
Benzalkonium Chloride	63449-41-2	264-151-6	<0.1*

*The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST AID MEASURES

First aid measures

Eye contact Rinse immediately with plenty of water and seek medical advice.

Skin Contact Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.

Inhalation Remove to fresh air.

Ingestion Consult a physician if necessary.

Chemical Name	Note to physicians
Trimethoprim	Serious hypersensitivity reactions have been reported with this product therapy. This product has been reported rarely to interfere with hematopoiesis, especially when administered in large doses and/or for prolonged periods.
Benzalkonium Chloride	Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Suitable extinguishing media
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media
None known.

Specific hazards arising from the chemical
Fire may produce irritating, corrosive and/or toxic gases.

Explosion data
Sensitivity to Mechanical Impact Not impact sensitive.
Sensitivity to Static Discharge Fine dust dispersed in air, in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Protective equipment and precautions for firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions Use personal protection recommended in Section 8. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing.

Environmental precautions See Section 12 for additional ecological information.

Methods for containment Prevent further leakage or spillage if safe to do so.

Methods for cleaning up Avoid creating dust.

7. HANDLING AND STORAGE

Advice on safe handling Avoid contact with skin, eyes or clothing. Avoid generation of dust. Do not eat, drink or smoke when using this product.

Storage Conditions Keep containers tightly closed in a dry, cool and well-ventilated place. Store away from incompatible materials.

Incompatible materials None known based on information supplied.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines This product, as supplied, does not contain any hazardous materials with occupational exposure limits established by the region specific regulatory bodies.

Chemical Name	ACGIH TLV	OSHA PEL	NIOSH IDLH	Allergan OEL
Trimethoprim 738-70-5	N/A	N/A	N/A	200

Appropriate engineering controls

Engineering Controls The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/face protection No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, safety glasses should be considered.

Skin and body protection During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. Use appropriate protective clothing for the task (e.g., lab coat, etc.).

Respiratory protection Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	Liquid	**Appearance**	Liquid
Color	No information available	**Odor**	No information available
Odor threshold	No information available		

Property	Values
pH	No information available
Melting point/freezing point	No information available
Boiling point / boiling range	No information available
Flash point	No information available
Evaporation rate	No information available

Flammability (solid, gas)	No information available
Flammability Limit in Air	
Upper flammability limit:	No information available
Lower flammability limit:	No information available
Vapor pressure	No information available
Vapor density	No information available
Specific Gravity	No information available
Water solubility	No information available
Solubility in other solvents	No information available
Partition coefficient	No information available
Autoignition temperature	No information available
Decomposition temperature	No information available
Explosive properties	No information available
Oxidizing properties	No information available

Other Information

Molecular weight	No information available
VOC Content (%)	No information available
Density	No information available
Bulk density	No information available

10. STABILITY AND REACTIVITY

Reactivity
Not defined As Reactive substance

Chemical stability
Stable under normal conditions.
Possibility of Hazardous Reactions
None under normal processing.
Conditions to avoid
Aerosol formation.
Incompatible materials
None known based on information supplied.
Hazardous Decomposition Products
None known based on information supplied.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Acute toxicity

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
SODIUM CHLORIDE USP	= 3000 mg/kg (Rat)	> 10 g/kg (Rabbit)	> 42 g/m³ (Rat) 1 h
Water	> 90 mL/kg (Rat)	N/A	N/A
Polymyxin B Sulfate	790 mg/kg (mouse)	N/A	N/A
Trimethoprim	1500 - 1850 mg/kg (Rat) > 5300 mg/kg (Rat)	N/A	N/A
Benzalkonium Chloride	N/A	= 1420 mg/kg (Rat)	N/A

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Chemical Name	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Effects on or via lactation
Polymyxin B Sulfate	No information available.	Long-term studies in animals to determine the carcinogenicity potential of this medication have not been conducted.	No information available.	It is not known whether the drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised

				when this drug is administered to nursing mothers.
Trimethoprim	This medication was demonstrated to be nonmutagenic in the Ames assay. In studies at two laboratories, no chromosomal damage was detected in cultured Chinese hamster ovary cells at concentrations approximately 500 times human plasma levels; at concentrations approximately 1000 times human plasma levels in the same cells, a low level of chromosomal damage was induced at one of the laboratories. No chromosomal abnormalities were observed in cultured human leukocytes at concentrations of this medication up to 20 times human steady-state plasma levels. No chromosomal effects were detected in peripheral lymphocytes of human subjects receiving 320 mg of trimethoprim in combination with up to 1600mg of sulfamethoxazole per day for as long as 112 weeks.	Long-term studies in animals to evaluate carcinogenic potential have not been conducted with Trimethoprim. The remaining components of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.	Teratogenic Effects - Pregnancy Category C This medication has been shown to be teratogenic in the rat when given in doses 40 times the human dose. In some rabbit studies, the overall increase in fetal loss (dead and resorbed and malformed conceptuses) was associated with doses six times the human therapeutic dose. While there are no large, well controlled studies on the use of this medication in pregnant women, Brumfitt and Pursell, in a retrospective study, reported the outcome of 186 pregnancies during which the mother received either placebo or this medication 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 this mediation 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 this medication and sulfamethoxazole at the time of conception or shortly thereafter. Because this medication may interfere with folic acid metabolism, it should be used during pregnancy only if the potential benefits justifies the potential risk to the fetus.	This medication is excreted in human milk. Because this medication may interfere with folic acid metabolism, caution should be exercised when this medication is administered to nursing women.
Benzalkonium Chloride	Not Suspected of being a Mutagen.	This product does not contain any carcinogens or potential carcinogens as listed by OSHA, IARC or NTP.	No information available.	No information available

Target Organ Effects Central nervous system, Eyes, Gastrointestinal tract (GI), kidney, Respiratory system, Skin.

Numerical measures of toxicity - Product Information

Unknown Acute Toxicity 1.58% of the mixture consists of ingredient(s) of unknown toxicity

The following values are calculated based on chapter 3.1 of the GHS document .

ATEmix (oral) 2797 mg/kg

ATEmix (dermal) 17518 mg/kg

12. ECOLOGICAL INFORMATION

Ecotoxicity

17.86% of the mixture consists of components(s) of unknown hazards to the aquatic environment

Chemical Name	Algae/aquatic plants	Fish	Crustacea
SODIUM CHLORIDE USP 7647-14-5	N/A	5560 - 6080: 96 h Lepomis macrochirus mg/L LC50 flow-through 12946: 96 h Lepomis macrochirus mg/L LC50 static 6020 - 7070: 96 h Pimephales promelas mg/L LC50 static 6420 - 6700: 96 h Pimephales promelas mg/L LC50 static 4747 - 7824: 96 h Oncorhynchus mykiss mg/L LC50 flow-through 7050: 96 h Pimephales promelas mg/L LC50 semi-static	1000: 48 h Daphnia magna mg/L EC50 340.7 - 469.2: 48 h Daphnia magna mg/L EC50 Static

Other adverse effects No information available

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated packaging Do not reuse container. Dispose of contents/containers in accordance with local regulations.

14. TRANSPORT INFORMATION

DOT Not regulated

TDG Not regulated

ICAO (air) Not regulated

IATA Not regulated

IMDG Not regulated

ADR Not regulated

ADN Not regulated

15. REGULATORY INFORMATION

International Inventories

TSCA	Not Listed
DSL/NDSL	Listed
EINECS/ELINCS	Listed

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List

EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances

US Federal Regulations

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

Acute health hazard	Yes
Chronic Health Hazard	No
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)

This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA

This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material

US State Regulations

California Proposition 65

This product does not contain any Proposition 65 chemicals

U.S. State Right-to-Know Regulations

Chemical Name	New Jersey	Massachusetts	Pennsylvania
Water 7732-18-5	-	-	X

16. OTHER INFORMATION

Revision Date 13-Jul-2016
Revision Note No information available

Disclaimer

The information provided in this Material Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

End of Safety Data Sheet