Material Safety Data Sheet

SULFAMETHOXAZOLE and TRIMETHOPRIM (SMX-TMP) Injection, USP

1. PRODUCT IDENTIFICATION

Product Name SULFAMETHOXAZOLE and TRIMETHOPRIM (SMX-TMP) Injection, USP
Product Use Medical Treatment; Antimicrobial
Manufacturer Teva Sicor Pharmaceuticals, Inc.
Address 11 Hughes
Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
1-202-483-7617 (International Collect)
Business Phone 1-800-729-9991
Website Address http:/ /www.newsicor.com

Common Names SMX-TMP
Chemical Name 4-Amino-N-(5-methyl-3-isoxazolyl) benzenesulfonamide) &
5-[(3,4,5-trimethoxyphenyl)methyl]-2,4-pyrimidinediamine
Chemical Formula $C_{10}H_{11}N_3O_3S$ and $C_{14}H_{18}N_4O_3$
Chemical Family Antibacterial

How Supplied 80 mg SMX/16 mg TMP per mL in 5 mL, 10 mL, and 30 mL vials

Date of Preparation: January 27, 2006

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	%	EXPOSURE LIMITS IN AIR				
			ACGIH		OSHA		Other
			TLV	CEIL	PEL	CEIL	
Sulfamethoxazole	723-46-6	8	NE	NE	NE	NE	NE
Trimethoprim	738-70-5	2	NE	NE	NE	NE	NE
Propylene Glycol	57-55-6	40	NE	NE	NE	NE	NE
Ethyl Alcohol	64-17-5	10	1000 ppm	NE	1000 ppm	NE	NE
Benzyl Alcohol	100-51-6	1	NE	NE	NE	NE	NE
Diethanolamine	111-42-2	<1	2 mg/m3-Skin	NE	NE	NE	NE
Sodium Metabisulfite	7681-57-4	<1	5 mg/m3	NE	NE	NE	NE
Water for Injection	7732-18-5	>37	NE	NE	NE	NE	NE

NE - Not Established C - Ceiling Limit

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 format

CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

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3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is a clear, pale yellow viscous solution. Eye and skin Irritant. Injection or ingestion in large quantities may be harmful. May cause allergic skin and/or respiratory reactions. May cause liver, blood or metabolic disturbances. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling.

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous infusion under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness and damage of the eyes and redness, itching, burning and skin damage. May cause allergic skin reactions.

Ingestion: Although ingestion is not an anticipated route of occupational exposure, this material has a moderate degree of toxicity if ingested. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including decreased urine volume, complete cessation of urine production, dermatitis, rash and systemic metabolic changes may occur. See package insert for other adverse reactions associated with therapeutic doses of this product.

Other: This product contains sodium metabisulfite and the symptoms of hypersensitivity or sulfite allergy may include rash, fever, respiratory difficulty or asthma-like symptoms.

Contains benzyl alcohol which is potentially toxic when administered locally to neural tissues. Benzyl alcohol has been reported to be associated with fatal “gasping syndrome” in premature infants.

Health Effects or Risks From Exposure **(An explanation in lay terms):**

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. Over-exposure may affect the kidney and the body’s ability to produce urine. Rash or other metabolic symptoms may occur. Allergy-like reactions may develop.

Cancer: Limited animal studies suggest this product may be carcinogenic, but no human data are available (see Section 11).

Chronic: Based on animal data, this material is not considered a reproductive toxicant (see Section 11).

Target Organs: Potential hazard to the liver and blood (see Section 11).

Pre-Existing Medical Conditions: Conditions aggravated by exposure may include skin, blood and liver disorders.

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4. FIRST-AID MEASURES

Skin Exposure: Remove contaminated shoes and clothing and flush affected area(s) with large amounts of water. If skin surface is damaged, apply a clean dressing and seek medical attention. If skin surface is not damaged, cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: Move victim away from exposure and into fresh air. If irritation or redness develops, flush eyes with clean water and seek medical attention. For direct contact, hold eyelids apart and flush the affected eye(s) with clean water for at least 15 minutes. Seek medical attention.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Victims of chemical exposure must be taken for medical attention. Take a copy of the MSDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians Desk Reference for additional treatment information.

5. FIRE-FIGHTING MEASURES

Flash Point: >200˚F Autoignition Temperature: Not applicable

Flammable Limits (in air by volume, %): Lower: Not applicable Upper: Not applicable

Fire Extinguishing Equipment: The size and nature of this product is such that it will not contribute to the intensity of a fire. Use extinguishing agent suitable for type of surrounding fire.

Water Spray: OK Carbon Dioxide: OK Halon: OK
Foam: OK Dry Chemical: OK Other: Any "ABC" Class

Unusual Fire and Explosion Hazards: When heated to decomposition, this product may emit toxic fumes containing oxides of nitrogen.

Explosion Sensitivity to Mechanical Impact: Not sensitive.
Explosion Sensitivity to Static Discharge: Not sensitive.

Special Fire Fighting Procedures: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.

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5. FIRE-FIGHTING MEASURES cont…

NFPA HAZARD CLASS:	Health:	1 (Slight)
	Flammability:	1 (Slight)
	Reactivity:	0 (Least)

6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay upwind and away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

7. HANDLING and STORAGE

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from any incompatible materials or conditions (see Section 10). Store at temperatures between 15°C and 30°C. Do not refrigerate.

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.

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8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances where air-purifying respirators may not provide adequate protection. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	Negligible	Evaporation Rate (n-BuAc=1):	NA
Specific Gravity (water = 1):	ND	Melting/Freezing Point:	NA
Solubility in Water:	Soluble	Boiling Point:	NA
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	3-5 in solution
Odor Threshold: ND			
Appearance and Color: Clear to yellow liquid			

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility. Keep away from acids, caustics and avoid extreme pH conditions.

Hazardous Polymerization: Will not occur.

Conditions To Avoid: Heat and contact with incompatible materials.

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11. TOXICOLOGICAL INFORMATION

Toxicity Data - Sulfamethoxazole:

Oral LD50(rat) =6200 mg/kg	IP LD50(rat) = 2690 mg/kg	SubQ LD50(rat) >5 g/kg
Oral LD50(mouse) = 2300 mg/kg	IV LD50(mouse) = 1460 mg/kg	SubQ LD50(mouse) > 5g/kg

Toxicity Data – Trimethoprim:

Oral LD50(rat) = 500 mg/kg	IP LD50 (rat) = 500 mg/kg	SubQ LD50 (rat) >5 g/kg
Oral LD50(mouse) = 2764 mg/kg	IP LD50 (mouse) = 400 mg/kg	SubQ LD50 (mouse) >5 g/kg
IV LD50 (mouse) = 132 mg/kg		

Suspected Cancer Agent: Long-term studies in animals to evaluate carcinogenic potential have not been conducted. However, sulfamethoxazole was tested by oral administration in one study in rats. It produced follicular-cell adenomas and carcinomas of the thyroid. It has not been listed as carcinogenic by NTP, IARC or OSHA.

Irritancy of Product: This product is expected to be irritating to contaminated skin, eyes and other tissues.

Sensitization to the Product: Sulfamethoxazole belongs to a class of drugs (sulfonamides) that are considered sensitizers. The combination product has been reported to cause allergic responses when given systemically.

Target Organ(s): Fatalities associate with administration of sulfonamides, although rare, have occurred due to severe reactions, including Steven-Johnson Syndrome, toxic epidermal necrolysis, fulminant heptatic necrosis, acranulocytosis, aplastic anemia and other blood dyscrasias.

Reproductive Toxicity Information: Listed below is information concerning the effects of Trimethoprim and Sulfamethoxazole on human and animal reproductive systems. This material is classified as a Pregnancy Category C: (Risk to Fetus Cannot be Ruled-Out)

Mutagenicity: Bacterial mutagenic studies have not been performed with sulfamethoxazole / trimethoprim in combination. Trimethoprim was demonstrated to be non-mutagenic 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 these 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 trimethoprim 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 1600 mg of sulfamethoxazole per day for as long as 112 weeks.

Embryotoxicity/Teratogenicity/ReproductiveToxicity: Negative for fertility impairment in rats treated with the combination of 350 mg/kg of sulfamethoxazole and 70 mg/kg of trimethoprim.

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11. TOXICOLOGICAL INFORMATION cont…

In rats, very high oral doses of 533 mg/kg sulfamethoxazole or 200 mg/kg trimethoprim produced teratologic effects manifested mainly as cleft palates. The highest dose which did not cause cleft palates in rats was 512 mg/kg sulfamethoxazole or 192 mg/kg trimethoprim when administered separately. In two studies in rats, no teratogenicity was observed when 512 mg/kg of sulfamethoxazole was used in combination with 128 mg/kg of trimethoprim. In one study, however, cleft palates were observed in one litter out of 9 when 355 mg/kg of sulfamethoxazole was used in combination with 88 mg/kg of trimethoprim. In some rabbit studies, an overall increase in fetal loss (dead and resorbed and malformed conceptuses) was associated with doses of trimethoprim 6 times the human therapeutic dose.

While there are no large, well-controlled studies on the use of sulfamethoxazole; trimethoprim in pregnant women, Brumfitt and Pursell as reported in the package labeling, in a retrospective study, studied the outcome of 186 pregnancies during which the mother received either placebo or oral sulfamethoxazole; trimethoprim. 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 sulfamethoxazole /trimethoprim. There were no abnormalities in the 10 pediatric patients whose mothers received the drug during the first trimester. In a separate survey, Brumfitt and Pursell also found no congenital abnormalities in 35 pediatric patients whose mothers had received oral sulfamethoxazole/trimethoprim at the time of conception or shortly thereafter.

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: This product will be relatively stable under ambient environmental conditions.

Effect of Materials on Plants or Animals: Studies indicate that this product should not cause significant impact on plants or animals.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect on plants or animals in the aquatic environment.

13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA “listed” or “characteristic” hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

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14. TRANSPORTATION INFORMATION

Proper Shipping Name: Not applicable
Hazard Class Number and Description: Not applicable
UN Identification Number: Not applicable
Packing Group: Not applicable
DOT Label(s) Required: Not applicable
North American Emergency Response Guidebook Number (1996): Not applicable.
MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable

15. REGULATORY INFORMATION

U.S. REGULATIONS

U.S. SARA Reporting Requirements: The component diethanolamine is subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. CERCLA Reportable Quantities (RQ): Not applicable

U.S. TSCA Inventory Status: Ciprofloxacin is a “drug” as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product does NOT contain a chemical known to the State of California to cause cancer or reproductive effects.

Other U.S. Federal Regulations: Based on this product’s use, the requirements of the OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS

Canadian DSL/NDSL Status: SULFAMETHOXAZOLE and TRIMETHOPRIM (SMX-TMP) is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): Eye and Skin Irritant. Injection or ingestion in large quantities may be harmful. May cause allergic skin and/or respiratory reactions. May cause liver, blood or metabolic disturbances. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling. This material should be administered under the supervision of a qualified physician. Do not eat, drink or smoke when handling this material. Clean up spills promptly.

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16. OTHER INFORMATION

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