ATTENTION!

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THIOTEA
Catalog Number: 1664000
Revision Date: December 13, 2010

SECTION 1 - PRODUCT AND COMPANY IDENTIFICATION

Common Name: Thiotepa
Manufacturer: U.S. Pharmacopeia
Responsible Party: Reference Standards Technical Services
Mailing Address: 12601 Twinbrook Parkway, Rockville, MD 20852 USA
Phone: 301-816-8129
Hours: 8 a.m. to 5 p.m. EST Mon. - Fri.

Product Use: USP Reference Standards and Authentic Substances are used for chemical tests and assays in analytical, clinical, pharmaceutical, and research laboratories.

SECTION 2 - HAZARD INFORMATION

EMERGENCY OVERVIEW - Cancer Suspect Agent, Poison, Reproductive Hazard

Adverse Effects: Adverse effects may include dizziness; drowsiness; fatigue; hives; loss of appetite; nausea and vomiting; missing menstrual periods; hair loss; bone marrow depression characterized by blood disorders (may take up to 30 days to appear); fever; chills; cough; blurred vision; sore throat or tightness; wheezing; headache; lower back or side pain; painful or difficult urination; unusual bleeding or bruising; pinpoint red spots on skin; bloody urine or black, tarry stools; joint pain; swollen feet or legs; and impaired fertility. Possible allergic reaction to material if inhaled, ingested, or in contact with skin.

Overdose Effects: Overdose of thiotepa may cause a decrease in the white blood cell count and/or platelets, increasing vulnerability to infection.

Acute: Irritating to eyes, gastrointestinal tract and respiratory tract. May be irritating to skin.

Chronic: Possible hypersensitization, skin depigmentation, contact allergic reactions, bone marrow depression and cancer (leukemia).

Medical Conditions Aggravated by Exposure: Hypersensitivity to material, bone marrow depression, chickenpox (including recent exposure), herpes zoster, history of gout or kidney stones, impaired liver or kidney function, and infection.

Cross Sensitivity: n/f

Target Organs: Blood and bone marrow

For additional information on toxicity, see Section 11.
Common Name: Thiopeta  
Formula: C6H12N3PS  
Synonym: Thiotriethylene phosphoramide; Triethylene thiophosphoramide; Tris(1-aziridinyl)phosphine sulphide  
Chemical Name: Aziridine, 1, 1', 1"-phosphinothioyldynetris-  
CAS: 52-24-4  
RTECS Number: SZ2975000  
Chemical Family: Ethylenimine (phosphorous derivative)  
Therapeutic Category: Antineoplastic; alkylating agent  
Composition: Pure material

SECTION 4 - FIRST AID MEASURES

Inhalation: Causes irritation. Remove to fresh air. 
Eye: Causes irritation. Flush with copious quantities of water for at least 15 minutes. 
Skin: May cause irritation and can be absorbed through the skin. Flush with copious quantities of soap and water. 
Ingestion: Causes irritation and toxicity. Flush out mouth with water. This material is unreliably and incompletely absorbed from the gastrointestinal tract. 

General First Aid Procedures: Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposures. In the United States, the national poison control center phone number is 1-800-222-1222. If person is not breathing, give artificial respiration. If breathing is difficult, give oxygen if available. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. 

Note to Physicians

Overdose Treatment: Overdose treatment should be symptomatic and supportive and may include the following: 
1. Monitor hemograms and WBC counts; transfusions of whole blood or platelets or leukocytes have proven beneficial in combating hematopoietic toxicity. 
2. Thiopeta is dialyzable. [PDR 55th ed. 2001]

SECTION 5 - FIREFIGHTING MEASURES

Extinguisher Media: Water spray, dry chemical, carbon dioxide, or foam as appropriate for surrounding fire and materials. 
Fire and Explosion Hazards: This material is assumed to be combustible. 
As with all dry powders, it is advisable to ground mechanical equipment in contact with dry material to dissipate the potential buildup of static electricity. 

Firefighting Procedures: As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing. 

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Spill Response: Wear approved respiratory protection, chemically compatible gloves, and protective clothing. Wipe up spillage or collect spillage using a high-efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labeled container for disposal, CAUTION: HAZARDOUS CHEMICAL WASTE. Wash spill site. 

SECTION 7 - HANDLING AND STORAGE

Handling: As a general rule, when handling USP Reference Standards, avoid all contact and inhalation of dust, mists, and/or vapors associated with the material. Clean equipment and work surfaces with suitable detergent or solvent after use. After removing gloves, wash hands and other exposed skin thoroughly. Use of a designated area is recommended for handling of potent
Storage: Store in tight container as defined in the USP-NF. This material should be handled and stored per label instructions to ensure product integrity.

SECTION 8 - EXPOSURE CONTROL / PERSONAL PROTECTION

Engineering Controls: Airborne exposure should be controlled primarily by engineering controls such as general dilution ventilation, local exhaust ventilation, or process enclosure. Local exhaust ventilation is generally preferred to general exhaust because it can control the contaminant at its source, preventing dispersion into the work area. An industrial hygiene survey involving air monitoring may be used to determine the effectiveness of engineering controls. Effectiveness of engineering controls intended for use with highly potent materials should be assessed by use of nontoxic surrogate materials.

Avoid any open handling of this material, particularly for grinding, crushing, weighing, or other dust-generating or aerosol-generating procedures. Use a laboratory fume hood, vented enclosure, glovebox, or other effective containment.

Respiratory Protection: Where respirators are deemed necessary to reduce or control occupational exposures, use NIOSH-approved respiratory protection and have an effective respirator program in place (applicable U.S. regulation OSHA 29 CFR 1910.134).

Gloves: Chemically compatible. For handling solutions, ensure that the glove material is protective against the solvent being used. Use handling practices that minimize direct hand contact. Employees who are sensitive to natural rubber (latex) should use nitrile or other synthetic nonlatex gloves. Use of powdered latex gloves should be avoided due to the risk of latex allergy. This material is extremely potent. To reduce the risk of contamination of skin and surfaces, wear two pairs of gloves. Remove the outer gloves after handling and cleanup of the material, and remove the inner gloves only after removing other personal protective equipment.

Eye Protection: Safety glasses with sideshields are recommended. Face shields or goggles may be required if splash potential exists or if corrosive materials are present. Approved eye protection (e.g., bearing the ANSI Z87 or CSA stamp) is preferred. Maintain eyewash facilities in the work area.

Protective Clothing: For handling of laboratory scale quantities, a disposable lab coat or isolation gown over street clothes is recommended. Where significant quantities are handled, work clothing and booties may be necessary to prevent take-home contamination.

Exposure Limits: Industry: 0.0014 mg/m³

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Properties as indicated on the MSDS are general and not necessarily specific to the USP Reference Standard Lot provided.

Appearance and Odor: Fine white crystalline flakes; odorless or faint odor.

Odor Threshold: n/f

pH: n/f

Melting Range: 51 - 57° C (decomposes at 40° C)

Boiling Point: n/f

Flash Point: n/f

Autoignition Temperature: n/f

Evaporation Rate: n/f

Upper Flammability Limit: n/f

Lower Flammability Limit: n/f

Vapor Pressure: n/f

Vapor Density: n/f

Specific Gravity: n/f

Solubility in Water: Freely soluble
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Fat Solubility: n/f

Other Solubility: Freely soluble in ethanol, in chloroform, and in ether; soluble in benzene.

Partition Coefficient: n-octanol/water: log P = 0.53

Percent Volatile: n/f

Reactivity in Water: n/f

Explosive Properties: n/f

Oxidizing Properties: n/f

Formula: C6H12N3PS

Molecular Weight: 189.22
SECTION 10 - STABILITY AND REACTIVITY

Conditions to Avoid: Avoid exposure to light and heat.
Incompatibilities: Acidic substances, strong oxidizing agents.
Decomposition Products: When heated to decomposition, material emits very toxic fumes of POx, SOx, and NOx. Emits toxic fumes under fire conditions.
Stable? Yes  Hazardous Polymerization? No

SECTION 11 - TOXICOLOGICAL PROPERTIES

Oral Rat: LD50: 23 mg/kg
Oral Mouse: LD50: 38 mg/kg
Other Toxicity Data: Oral Quail: LD50: 237 mg/kg
Irritancy Data: Skin/human: reaction not reported (Std. Draize test; 2 mg/3 weeks)
Corrosivity: n/f
Sensitization Data: n/f
Listed as a Carcinogen by: NTP: Yes  IARC: Yes  OSHA: No
Other Carcinogenicity Data: NCI Carcinogenesis Bioassay results: Positive in mouse and rat.
NTP: Known to be a human carcinogen.
IARC: Carcinogenic to humans.
Exposure to thiotepa is associated with leukemia in humans; studies in animals demonstrated carcinogenicity at multiple sites.

Mutagenicity Data: Thiotepa was mutagenic in in vitro assays in Salmonella typhimurium, E. coli, Chinese hamster lung and human lymphocytes. Chromosomal aberrations and sister chromatid exchanges were observed in vitro with thiotepa in bean root tips, human lymphocytes, Chinese hamster lung, and monkey lymphocytes. Mutations were observed with oral thiotepa in mice at doses >2.5 mg/kg (8mg/m2). The mouse micronucleus test was positive with IP administration of >1 mg/kg (3.2 mg/m2). Other positive in vitro chromosomal aberration or mutation assays included Drosophia melanogaster, Chinese hamster marrow, murine marrow, monkey lymphocyte, and murine germ cell.

Reproductive and Developmental Effects: Antineoplastic therapy may impair male or female fertility. Exposure to antineoplastic therapy during pregnancy may increase the risk of birth defects or growth retardation. Thiotepa given by the IP route was teratogenic in mice at doses greater than 1 mg/kg and in rats at doses greater than 3 mg/kg. It was also lethal to rabbit fetuses at a dose of 3 mg/kg.

SECTION 12 - ECOLOGICAL INFORMATION

Ecological Information: n/f

SECTION 13 - DISPOSAL CONSIDERATIONS

Disposal: Place material in a thick plastic hazardous waste disposal bag or leak proof container and label it CAUTION: HAZARDOUS CHEMICAL WASTE. Dispose of waste in accordance with all applicable Federal, State, and local laws. Alternatively, chemical destruction may be used, especially for small quantities in a laboratory setting. Alkylation agents such as thiotepa can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxy ions, ammonia, thiol and thiosulfate. To facilitate completion of reaction, dissolve the agent in ethanol or a similar solvent. Before disposal, check for residual compound by reaction with 4(4-nitrobenzyl)-pyridine.

SECTION 14 - TRANSPORT INFORMATION

Shipping Name: Toxic solid, organic, n.o.s. (Thiotepa)
THIOTEPA

Class: 6.1
UN Number: UN2811
Packing Group: II
Additional Transport Information: n/f

SECTION 15 - REGULATORY INFORMATION

U.S. Regulatory Information: n/f
International Regulatory Information: EINECS # 200-135-7
California Proposition 65: Carcinogen

SECTION 16 - OTHER INFORMATION

Revision: 13-Dec-10
Previous Revision Date: 10-Mar-05