Material Safety Data Sheet

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METHOTREXATE
Catalog Number: 1414003
Revision Date: June 1, 2010

SECTION 1 - PRODUCT AND COMPANY IDENTIFICATION

Common Name: Methotrexate
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


Adverse Effects: Adverse effects may include nausea, vomiting, diarrhea, stomach pain, mouth sores or inflammation, fever, chills, dizziness, tiredness, cough, skin rash, and hair loss. Possible allergic reaction to material if inhaled, ingested, or in contact with skin.

Overdose Effects: Overdose may cause the adverse effects listed above as well as mood and mental changes, troubled breathing, seizures, and kidney failure.

Acute: Possible eye, skin, gastrointestinal, and/or respiratory tract irritation.

Chronic: Possible hypersensitization, bone marrow depression and blood disorders, gastrointestinal bleeding, liver damage, kidney damage, impaired fertility, lung problems, and cancer.

Medical Conditions Aggravated by Exposure: Hypersensitivity to material, active alcoholism, ascites, pleural or peritoneal effusions, impaired liver or kidney function, bone marrow depression, immunodeficiency, infection, chickenpox (existing or recent), herpes zoster, oral mucositis, peptic ulcer or ulcerative colitis, previous cytotoxic drug or radiation therapy, diabetes, risk of osteoporosis, and lung disease.

Cross Sensitivity: n/f
Target Organs: Bone marrow

For additional information on toxicity, see Section 11.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

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Common Name: Methotrexate

Formula: C20H22N8O5

Synonym: Amethopterin; 4-Amino-10-methylfolic acid

Chemical Name: L-Glutamic acid, N-[4-[(2,4-diamino-6-pteridinyl) methyl]methylamino]benzoyl]-

CAS: 59-05-2

RTECS Number: MA1225000

Chemical Family: Pteridine; alicyclic carboxylic acid

Therapeutic Category: Antineoplastic antimetabolite; antirheumatic; folic acid antagonist

Composition: Pure material

### SECTION 4 - FIRST AID MEASURES

**Inhalation:** May cause irritation. Remove to fresh air.

**Eye:** Causes irritation. Flush with copious quantities of tepid water for at least 15 minutes.

**Skin:** Causes irritation. Flush with copious quantities of soap and water for at least 15 minutes.

**Ingestion:** May cause irritation and toxicity. Flush out mouth with water. This material is readily 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. Administer activated charcoal as a slurry. Perform gastric lavage after first protecting airway and controlling seizures.
2. Administer leucovorin as soon as possible, preferably within the first hour of overdose, to reverse toxic effects of methotrexate. This may be combined with IV thymidine.
3. Intravenous glucarpidase may be combined with leucovorin and thymidine to catabolize methotrexate to inactive metabolites.
4. After assuring adequate hydration and renal function, initiate urinary alkalization with sodium bicarbonate and potassium chloride to prevent precipitation of methotrexate and metabolites in renal tubules. [Meditext 2010]

### 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 with dampened toweling. Avoid breathing dust. Surfaces contaminated with methotrexate should be washed repeatedly with 5% ammonium hydroxide and rinsed with soap and water. Place spillage and all contaminated cleanup materials in a thick plastic hazardous waste disposal bag or leakproof container and label it CAUTION: HAZARDOUS CHEMICAL WASTE.
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 materials.

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: 0.3 micrograms/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: Yellow to orange-brown crystalline powder; odorless.

Odor Threshold: n/f

pH: 8.5 - 8.8

Melting Range: 185 - 204° C (decomposes)

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: Practically insoluble
Fat Solubility: n/f
Other Solubility: Practically insoluble in ethanol, in chloroform, and in ether; freely soluble in dilute solutions of alkali hydroxides and carbonates; slightly soluble in 6 N hydrochloric acid.
Partition Coefficient: n-octanol/water: n/f
Percent Volatile: n/f
Reactivity in Water: n/f
Explosive Properties: n/f
Oxidizing Properties: n/f
Formula: C20H22N8O5
Molecular Weight: 454.44
SECTION 10 - STABILITY AND REACTIVITY

Conditions to Avoid: Light, heat, and moisture.

Incompatibilities: Strong oxidizing agents and strong acids.

Decomposition Products: When heated to decomposition, material emits toxic fumes including NOx. Emits toxic fumes under fire conditions.

Stable? Yes Hazardous Polymerization? No

SECTION 11 - TOXICOLOGICAL PROPERTIES

Oral Rat: LD50: 135 mg/kg
Oral Mouse: LD50: 146 mg/kg
Other Toxicity Data: n/f
Irritancy Data: n/f
Corrosivity: n/f
Sensitization Data: n/f

Listed as a Carcinogen by: NTP: No IARC: No OSHA: No

Other Carcinogenicity Data: This material is not classifiable as to its carcinogenicity in humans. Secondary malignancies are potential delayed effects of many antineoplastic agents, although it is not clear whether the effect is related to their mutagenic or immunosuppressive action. The effect of dose and duration of therapy is also unknown, although risk seems to increase with long-term use. Methotrexate was not carcinogenic in lifetime studies in Swiss mice or Syrian golden hamsters. However, in later studies in mice it induced tumors of the sense organs and was an equivocal tumorigenic agent for producing tumors of the respiratory system and blood.

Mutagenicity Data: Methotrexate inhibited DNA synthesis in humans and mice in vivo, in human and mouse lymphocytes, and hamster ovary cells in vitro. It caused DNA damage in human leukocytes, mouse leukocytes and fibroblasts, and in mice in vivo. It induced DNA repair in hamster ovary cells, B. subtilis, and E. coli, and induced unscheduled DNA synthesis in human HeLa cells in vitro. It was not mutagenic in the Salmonella/microsome assay, and did not induce thioguanine-resistant mutations in Chinese hamster V79 cells in vitro. Workers occupationally exposed to methotrexate had a higher rate of micronuclei and gene mutations in their peripheral lymphocytes than unexposed controls.

Reproductive and Developmental Effects: Reversible sterility (reduction in sperm production) has been seen in men receiving methotrexate therapeutically. Miscarriage and birth defects have been reported with therapeutic use in women, particularly in the first trimester. These birth defects may include eye, ear, or facial abnormalities, skeletal defects, and central nervous system abnormalities. Adverse effects with doses as low as 2.5 mg/day for five days have been documented. Rats given 0.2 to 0.3 mg/kg doses of methotrexate during gestation had 64% resorptions and 30% malformations. Rabbits given oral doses of 0.5 mg/kg during gestation had an increased incidence of miscarriage and structural defects in the offspring, and cats given 0.5 mg/kg/day during gestation had maternal toxicity, embryo lethality, and an increase in birth defects. In mice, 10 mg/kg intraperitoneal doses increased resorptions but not malformations, and 25 or 50 mg/kg doses induced malformations. 30 mg/kg intravenous doses in monkeys retarded embryonic growth but did not increase malformations.

SECTION 12 - ECOLOGICAL INFORMATION

Ecological Information: n/f

SECTION 13 - DISPOSAL CONSIDERATIONS
Disposal: Place material in a thick plastic hazardous waste disposal bag or leakproof container and label it CAUTION: HAZARDOUS CHEMICAL WASTE. Dispose of waste in accordance with all applicable Federal, State, and local laws.

SECTION 14 - TRANSPORT INFORMATION

Shipping Name: Toxic solid, organic, n.o.s. (Methotrexate)
Class: 6.1
UN Number: UN2811
Packing Group: III
Additional Transport Information: n/f

SECTION 15 - REGULATORY INFORMATION

U.S. Regulatory Information: California Proposition 65: Developmental Toxicity
International Regulatory Information: EINECS#: 200-413-8

SECTION 16 - OTHER INFORMATION

Revision: 01-Jun-10
Previous Revision Date: 18-Apr-06