



Material Safety Data Sheet

12601 Twinbrook Parkway,
Rockville, MD 20852 USA

Phone Calls: 301-816-8129
8 a.m. to 5 p.m. EST Mon. - Fri.

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FLUOROURACIL

Catalog Number: 1279000

Revision Date:

July 1, 2007

SECTION 1 - PRODUCT AND COMPANY IDENTIFICATION

Common Name: Fluorouracil

Manufacturer: U. S. Pharmacopeia

Responsible Party: Reference Standards Technical Services

Mailing Address: 12601 Twinbrook Parkway, Rockville, MD 20852 USA

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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. Toxic. Reproductive Hazard. Irritant.

Adverse Effects: Adverse effects may include stomach cramps; nausea or vomiting; heartburn; diarrhea; fever; chills; cough or hoarseness; lower back or side pain; painful or difficult urination; sores in mouth or on lips; black, tarry stools; blood in urine or stools; unusual bleeding or bruising; pinpoint red spots on skin; skin rash, dryness, or itching; hair loss; loss of appetite; weakness; tingling sensation in hands and feet; visual changes or tearing; and confusion. Possible allergic reaction to material if inhaled, ingested or in contact with skin.

Overdose Effects: n/f

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

Chronic: Possible hypersensitization, bone marrow depression, and cancer.

Medical Conditions Aggravated by Exposure: Hypersensitivity to material, history or heart disease, impaired liver or kidney function, infection, bone marrow depression, tumor cell infiltration of bone marrow, chickenpox (including recent exposure), herpes zoster, dihydropyrimidine dehydrogenase (DPD) enzyme deficiency, and previous cytotoxic drug therapy with alkylating agents or high-dose pelvic radiation therapy.

Cross Sensitivity: n/f

Target Organs: Bone marrow

For additional information on toxicity, see Section 11.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

FLUOROURACIL

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Common Name: Fluorouracil

Formula: C₄H₃FN₂O₂

Synonym: 5-Fluorouracil; 5-FU

Chemical Name: 2,4(1H,3H)-Pyrimidinedione, 5-fluoro-

CAS: 51-21-8

RTECS Number: YR0350000

Chemical Family: Pyrimidine analog

Therapeutic Category: Antineoplastic

Composition: Pure Material

SECTION 4 - FIRST AID MEASURES

Inhalation: May cause irritation. Remove to fresh air.

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

Skin: Causes irritation and possibly inflammatory or photosensitivity reactions. Avoid contact. Flush with copious quantities of soap and water. Small amounts of this material may be absorbed through the skin, and absorption is increased if skin is ulcerated or inflamed.

Ingestion: May cause irritation and toxicity. Flush out mouth with water. This material is poorly absorbed from the gastrointestinal tract.

General First Aid Procedures: Remove from exposure. Remove contaminated clothing. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. If person is not breathing give artificial respiration. If breathing is difficult give oxygen. Obtain medical attention.

Note to Physicians

Overdose Treatment: Treatment of overdose should be symptomatic and supportive and may include the following:

1. Perform gastric lavage soon after ingestion. Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
2. Administer activated charcoal as a slurry.
3. Monitor for bone marrow toxicity, bleeding tendency, and infection. Septicemia may be a fatal complication. Monitor electrolytes for possible depletion due to vomiting or diarrhea.
4. Allopurinol may reduce the dose-limiting toxicity of high-dose fluorouracil.
5. Uridine rescue may reduce toxicity of high-dose fluorouracil. [Meditext 2007]

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. Wash spill site. 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. Wash thoroughly after handling.

Storage: Store in tight, light-resistant 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: Engineering controls such as exhaust ventilation are recommended.

Respiratory Protection: Use a NIOSH-approved respirator, if it is determined to be necessary by an industrial hygiene survey involving air monitoring. If a respirator is not required, an approved dust mask should be used.

Gloves: Chemically compatible

Eye Protection: Safety glasses or goggles

Protective Clothing: Protect exposed skin.

Exposure Limits: n/f

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: White to nearly white crystalline powder; practically odorless

Odor Threshold: n/f

pH: 4.5 - 5.0 (1% aqueous solution)

Melting Range: 282 - 283° C (decomposes)

Boiling Point: 190 - 200° C (sublimes)

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: Sparingly soluble

Fat Solubility: n/f

Other Solubility: Slightly soluble in alcohol; practically insoluble in chloroform and in ether

Partition Coefficient: n-octanol/water: -0.89

Percent Volatile: n/f

Reactivity in Water: n/f

Explosive Properties: n/f

Oxidizing Properties: n/f

Formula: C₄H₃FN₂O₂

Molecular Weight: 130.08

SECTION 10 - STABILITY AND REACTIVITY

Conditions to Avoid: Avoid exposure to light and extreme heat.

Incompatibilities: Strong bases, strong oxidizing agents

Decomposition Products: When heated to decomposition material emits toxic fumes of F- and NOx. Emits toxic fumes under fire conditions.

Stable? Yes **Hazardous Polymerization?** No

SECTION 11 - TOXICOLOGICAL PROPERTIES

Oral Rat: LD50: 230 mg/kg

Oral Mouse: LD50: 115 mg/kg

Other Toxicity Data: Oral Dog LD50: 30 mg/kg

Irritancy Data: Rabbit/skin (0.5%): mild; Rabbit/eye (0.5%): mild

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 to 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. Antimetabolites have been shown to be carcinogenic in animals and may be associated with an increased risk of development of secondary carcinomas in humans. There was no evidence of carcinogenicity in small groups of rats given fluorouracil orally at doses up to 3 mg/rat, five days a week for 52 weeks, or in male rats administered 33 mg/kg intravenously once a week for 52 weeks. Female mice given 1 mg fluorouracil intravenously once a week for 16 weeks experienced no effect on the incidence of lung adenomas.

Mutagenicity Data: Fluorouracil was positive in three in vitro cell neoplastic transformation assays. No evidence of mutagenic activity was observed in the Ames Salmonella assay, but it was shown to be mutagenic in the survival count rec-assay with *B. subtilis* and in the *Drosophila* wing-hair spot test. Fluorouracil produced petite mutations in *Saccharomyces cerevisiae* and was positive in the micronucleus test in mouse bone marrow cells. It was clastogenic in vitro in Chinese hamster fibroblasts and has been shown to increase sister chromatid exchanges in vitro in human lymphocytes. Fluorouracil has been reported to increase numerical and structural chromosome aberrations in peripheral lymphocytes in treated patients.

Reproductive and Developmental Effects: In several studies, birth defects have been reported in children whose mothers were treated with fluorouracil therapeutically during pregnancy. Antineoplastic therapy can adversely affect male and female fertility through gonadal suppression, resulting in the absence of menstruation or sperm. The effects appear to be related to dose and length of therapy and may be irreversible. Chromosomal changes in spermatogonia occurred in male rats given intraperitoneal doses of 125 or 250 mg/kg. In female rats, fluorouracil given in intraperitoneal doses of 25 or 50 mg/kg/week for 3 weeks adversely affected the incidence of fertile matings, pre- and post-implantation embryo development, the incidence of pre-implantation death, and the incidence of embryo chromosomal anomalies. Fluorouracil exhibited maximum teratogenicity when given to mice as a single injection of 10 or 40 mg/kg. Birth defects (cleft palate, skeletal defects, deformed appendages, paws, or tails) and embryotoxicity occurred in rats given intraperitoneal doses of fluorouracil at 12 to 37 mg/kg and in hamsters given 3 to 9 mg/kg.

SECTION 12 - ECOLOGICAL INFORMATION

FLUOROURACIL**Catalog Number:** 1279000**Revision Date:**July 1, 2007

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. (Fluorouracil)**Class:** 6.1**UN Number:** UN2811**Packing Group:** III**Additional Transport Information:** n/f

SECTION 15 - REGULATORY INFORMATION
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U.S. Regulatory Information: California Proposition 65: Developmental Toxicity**International Regulatory Information:** EINECS # 200-085-6

Hazard Code: T

Risk Phrases: R26/27/28, R46, R61, R60

Safety Phrases: S45, S26, S27, S36/37/39

SECTION 16 - OTHER INFORMATION

Revision: 01-Jul-07**Previous Revision Date:** 18-Dec-03