SAFETY DATA SHEET

Product Name: Fluorouracil Injection, USP

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Name And Address	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA	Hospira Australia Pty Ltd 1 Lexia Place Mulgrave VIC 3170 AUSTRALIA
Emergency Telephone	CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia - 61-290372994; UK - 44-870-8200418	
Hospira, Inc., Non-Emergency	224 212-2000	
Product Name	Fluorouracil Injection, USP	
Synonyms	2,4 (1H, 3H)-pyrimidinedione, 5-fluoro-5-fluorouracil.	

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Fluorouracil Injection, USP, is a solution containing 5-fluorouracil, an analog of the pyrimidine uracil. It is an anti-neoplastic used in the treatment of some types of cancer. It may also be used topically for treating malignant or pre-malignant lesions of the skin. It is cytotoxic, neurotoxic, and in the workplace, should also be considered a potential occupational reproductive hazard, harmful to the fetus, potentially irritating to the skin, eyes and respiratory tract, and a photosensitizer. Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, and cardiovascular system.

U.S. OSHA GHS Classification

	Hazard Class	Hazard Category
Physical Hazards	Not Classified	Not Classified
Health Hazards	**Hazard Class**	**Hazard Category**
	Toxic to Reproduction	1
	Germ Cell Mutagenicity	2
	STOT – RE	2

Label Element(s)

Pictogram

Signal Word

Danger

Hazard Statement(s)

May damage fertility or the unborn child
Suspected of causing genetic defects
May cause damage to organs through prolonged or repeated exposure

Precautionary Statement(s)

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical

attention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name 5-Fluorouracil
Chemical Formula $C_4H_3FN_2O_2$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
5-Fluorouracil	2.5-5	51-21-8	YR0350000

Non-hazardous ingredients include Water for Injection. Sodium hydroxide may be added to adjust the pH.

4. FIRST AID MEASURES

Eye Contact Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Skin Contact Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/ supportive care as necessary.

Inhalation Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

Ingestion Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

5. FIRE FIGHTING MEASURES

Flammability None anticipated for this aqueous product.

Fire & Explosion Hazard None anticipated for this aqueous product.

Extinguishing Media As with any fire, use extinguishing media appropriate for primary cause of fire such as carbon dioxide, dry chemical extinguishing powder or foam.

Special Fire Fighting Procedures No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal Isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable material and clean affected area with soap and water. Dispose of spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling 5-fluorouracil is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic anti-neoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic anti-neoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. Precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this anti-neoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is required when working with this material.

7. HANDLING AND STORAGE: continued

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for anti-neoplastic agents. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

No special precautions required for hazard control. Persons with known hypersensitivities to this material, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling open containers of this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure Limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
5-Fluorouracil	8-hr TWA: Not established	8-hr TWA: Not established	8-hr TWA: Not Established	8-hr TWA: Not Established

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit
ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.
AIHA WEEL: Workplace Environmental Exposure Level
EEL: Employee Exposure Limit.
TWA: 8 hour Time Weighted Average.

Respiratory Protection

Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. Since protection provided by air purifying respirators is limited, a powered air purifying respirator or supplied air should be considered during an uncontrolled release event if exposure levels are not known, or during events 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 require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Skin Protection

When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to chemotherapeutic agents. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

Eye Protection

Eye protection is normally not required during intended product use. However, if eye contact is likely to occur, the use of chemical safety goggles (as a minimum) is recommended.

Engineering Controls

Local exhaust ventilation may be used to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A sterile, non-pyrogenic injectable solution in a vial.
Odor	NA
Odor Threshold	NA
pH	8.6 to 9.4
Melting point/Freezing Point	NA
Initial Boiling Point/Boiling Point Range	NA
Flash Point	NA
Evaporation Rate	NA
Flammability (solid, gas)	NA
Upper/Lower Flammability or Explosive Limits	NA
Vapor Pressure	NA
Vapor Density (Air =1)	NA
Relative Density	NA
Solubility	NA
Partition Coefficient: n-octanol/water	NA
Auto-ignition Temperature	NA
Decomposition Temperature	NA
Viscosity	NA

10. STABILITY AND REACTIVITY

Reactivity	Not determined.
Chemical Stability	Stable under recommended storage conditions and use. Active ingredient reported to be light sensitive.
Hazardous Reactions	Not determined
Conditions to Avoid	Not determined
Incompatibilities	Not determined
Hazardous Decomposition Products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx), nitrogen oxides (NOx), and hydrogen fluoride.
Hazardous Polymerization	Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity - Not determined for the product formulation. Information for the active ingredient is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
5-Fluorouracil	100	LD50	Oral Oral Oral Oral	230 115 18.9 30	mg/kg mg/kg mg/kg mg/kg	Rat Mouse Rabbit Dog
5-Fluorouracil	100	LD50	Intravenous	245 81 25	mg/kg mg/kg mg/kg	Rat Mouse Guinea Pig
5-Fluorouracil	100	LD50	Intraperitoneal	70 100	mg/kg mg/kg	Rat Mouse

LD 50: Dosage that produces 50% mortality.

11. TOXICOLOGICAL INFORMATION: continued

Occupational Exposure Potential	Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact. There is increasing evidence that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these agents if workplace exposures are not properly controlled. The actual risk in the workplace is not known.
Signs and Symptoms	None anticipated from normal handling of this product. In clinical use, adverse effects may include bone marrow and gastrointestinal toxicity. Adverse effects on bone marrow include leucopenia, thrombocytopenia, and anemia. Adverse gastrointestinal effects may include nausea, vomiting, stomatitis, gastrointestinal ulceration and bleeding, diarrhea, or hemorrhage. Rashes and alopecia are also common. Ocular irritation, central neurotoxicity (cerebellar ataxia), and myocardial ischemia have also occurred. Topical application of solutions or creams with 1-5% fluorouracil caused skin irritation and allergic skin reactions. These solutions or creams can also cause eye irritation. Dermatitis and, rarely, erythema multiforme have been reported.
Aspiration Hazard	None anticipated from normal handling of this product.
Dermal Irritation/Corrosion	None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with redness and discomfort.
Ocular Irritation/Corrosion	None anticipated from normal handling of this product. However, inadvertent eye contact of this product with eyes may produce irritation with stinging, redness, watering, and discomfort.
Dermal or Respiratory Sensitization	None anticipated from normal handling of this product. In clinical topical use, dermatitis is most often seen as a pruritic maculopapular rash usually appearing on the extremities and less frequently on the trunk. Rarely, anaphylaxis and generalized allergic reactions have been reported during clinical use. In addition, this material is a photosensitizer. Exposure to sunlight can cause an exaggerated sunburn-like reaction.
Reproductive Effects	None anticipated from normal handling of this product. Fluorouracil has been shown to impair fertility after parenteral administration in rats. Intraperitoneal dosages of 125 to 250 mg/kg induced chromosomal aberrations and changes in chromosome organization of spermatogonia in rats. Spermatogonial differentiation was also inhibited by fluorouracil, resulting in transient infertility. However, in studies with a strain of mouse which is sensitive to the induction of sperm head abnormalities, 5-fluorouracil was inactive at oral dosages of 5 to 80 mg/kg/day. In female rats, intraperitoneal fluorouracil at dosages of 25 and 50 mg/kg during the preovulatory phase of oogenesis significantly reduced the incidence of fertile matings, delayed the development of preimplantation and post-implantation embryos, increased the incidence of preimplantation lethality and induced chromosomal anomalies in these embryos. Single dose intravenous and intraperitoneal injections of 5-fluorouracil have been reported to kill differentiated spermatogonia and spermatocytes (at 500 mg/kg) and to produce abnormalities in spermatids (at 50 mg/kg) in mice. Fluorouracil, given parenterally, has been shown to be teratogenic in mice, rats, and hamsters when given at doses equivalent to the usual human intravenous dose. Fluorouracil exhibited maximum teratogenicity when given to mice as single intraperitoneal injections of 10 to 40 mg/kg on Day 10 or 12 of gestation. Similarly, intraperitoneal dosages of 12 to 37 mg/kg given to rats between Days 9 and 12 of gestation and intramuscular doses of 3 to 9 mg/kg given to hamsters between Days 8 and 11 of gestation were teratogenic and/or embryotoxic (e.g. resulted in increased resorptions or embryolethality). In monkeys, divided dosages of 40 mg/kg given between Days 20 and 24 of gestation were not teratogenic. Dosages higher than 40 mg/kg resulted in abortion. The amount of fluorouracil absorbed systemically after

topical administration to actinic keratoses is minimal.

11. TOXICOLOGICAL INFORMATION: continued

Mutagenicity	Oncogenic transformation of fibroblasts from mouse embryo has been induced *in vitro* by fluorouracil, but the relationship between oncogenicity and mutagenicity is not clear. Fluorouracil has been shown to be mutagenic to several strains of *Salmonella typhimurium*, including TA 1535, TA 1537 and TA 1538, and to *Saccharomyces cerevisiae*, although no evidence of mutagenicity was found with *Salmonella typhimurium* strains TA 92, TA 98 and TA 100. In addition, a positive effect was observed in the micronucleus test on bone marrow cells of the mouse, and fluorouracil at very high concentrations produced chromosomal breaks in hamster fibroblasts *in vitro*. Fluorouracil was clastogenic *in vitro* in Chinese hamster fibroblasts at concentrations of 1.0 and 2.0 ug/mL and has been shown to increase sister chromatid exchange in vitro in human lymphocytes. In addition, 5-fluorouracil has been reported to produce an increase in numerical and structural chromosome aberrations in peripheral lymphocytes of patients treated with this product.
Carcinogenicity	Long-term studies in animals to evaluate the carcinogenic potential of fluorouracil have not been conducted. However, there was no evidence of carcinogenicity in small groups of rats given fluorouracil orally at doses of 0.01, 0.3, 1 or 3 mg per rat 5 days per week for 52 weeks, followed by a six-month observation period. Also, in other studies, 33 mg/kg of fluorouracil was administered intravenously to male rats once a week for 52 weeks followed by observation for the remainder of their lifetimes with no evidence of carcinogenicity. Female mice were given 1 mg of fluorouracil intravenously once a week for 16 weeks with no effect on the incidence of lung adenomas.
Carcinogen Lists	**IARC:** Group 3 – not classifiable **NTP:** Not listed **OSHA:** Not listed
Specific Target Organ Toxicity – Single Exposure	NA
Specific Target Organ Toxicity – Repeat Exposure	Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, and cardiovascular system.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity	Not determined for product. EC50(16hr) = 0.027 mg/L in Pseudomonas putida for 5-fluorouracil. EC50(24hr) = 0.12 mg/L in Vibrio fisheri for 5-fluorouracil. EC50(96hr) = 0.11 mg/L in Pseudokirchneriella subcapitata for 5-fluorouracil. EC50(48hr) = 36 mg/L in Daphnia magna for 5-fluorouracil. LOEC(120 hr growth) = 400 mg/L in Pimephales promelas for 5-fluorouracil.
Persistence/Biodegradability	Not determined for product.
Bioaccumulation	Not determined for product.
Mobility in Soil	Not determined for product.

Notes:
1. LC50: Concentration in water that produces 50% mortality in fish.
2. EC50: Concentration in water that produces 50% inhibition of growth in algae.

13. DISPOSAL CONSIDERATIONS

Waste Disposal	All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements.
Container Handling and Disposal	Dispose of container and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS	Regulated, if shipment of single or inner packagings are >5L liquids, or >5KG of solids.
Proper Shipping Name	Environmentally hazardous substance, liquid, n.o.s. (5-Fluorouracil)
Hazard Class	9
UN Number	UN3082
Packing Group	III
Reportable Quantity	N/A
ICAO/IATA STATUS	Regulated, if shipment of single or inner packagings are >5L liquids, or >5KG of solids.
Proper Shipping Name	Environmentally hazardous substance, liquid, n.o.s. (5-Fluorouracil)
Hazard Class	9
UN Number	UN3082
Packing Group	III
Reportable Quantity	N/A
IMDG STATUS	Regulated, if shipment of single or inner packagings are >5L liquids, or >5KG of solids.
Proper Shipping Name	Environmentally hazardous substance, liquid, n.o.s. (5-Fluorouracil)
Hazard Class	9
UN Number	UN3082
Packing Group	III
Reportable Quantity	N/A
Transport Comments:	Shipments of single or inner packagings of < or = 5L liquids, or < or = 5KG solids are not regulated as long as the general packaging provisions are met

15. REGULATORY INFORMATION

US TSCA Status	This product is exempt. However, 5-fluorouracil is listed on the TSCA inventory.
US CERCLA Status	Not listed
US SARA 302 Status	Listed - 500 lb TPQ (lower threshold); 10000 lb TPQ (upper threshold)
US SARA 313 Status	Listed - Subject to the reporting requirements of Section 313 of SARA Title III and 40 CFR
US RCRA Status	Not listed
US PROP 65 (Calif.)	This product is, or contains chemical(s) known to the State of California to cause developmental toxicity.

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

15. REGULATORY INFORMATION: continued

GHS/CLP Classification*

*In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

Prevention

Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Wear protective gloves/protective clothing/eye protection/face protection
Do not breathe vapor or spray
Wash hands thoroughly after handling
Avoid release into the environment

Response

If exposed or concerned: Get medical advice/attention. Get medical attention if you feel unwell.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.

Collect spillage. Avoid release into the environment.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.

Classification(s) NA
Symbol NA
Indication of Danger NA
Risk Phrases NA
Safety Phrases
S23: Do not breathe vapor/spray
S24: Avoid contact with the skin
S25: Avoid contact with eyes
S37/39 Wear suitable gloves and eye/face protection
S61: Avoid release into the environment

16. OTHER INFORMATION

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD_{50}	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
STEL	15-minute Short Term Exposure Limit
STOT - SE	Specific Target Organ Toxicity – Single Exposure
STOT - RE	Specific Target Organ Toxicity – Repeated Exposure
TSCA	Toxic Substance Control Act

TWA	8-hour Time Weighted Average

16. OTHER INFORMATION: continued

MSDS Coordinator: Hospira GEHS
Date Prepared: June 19, 2013
Date Revised: January 5, 2015

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