MATERIAL SAFETY DATA SHEET

Product Name: Fluorouracil Injection, USP

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address
Hospira Inc.
275 North Field Drive
Lake Forest, Illinois USA
60045

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 (02) 8014 4880

Hospira, Inc., Non-Emergency 224-212-2000

Product Name Fluorouracil Injection, USP

Synonyms 2,4 (1H, 3H)-pyrimidinedione, 5-fluoro-5-fluorouracil

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name 5-Fluorouracil

Chemical Formula \( \text{C}_4\text{H}_3\text{FN}_2\text{O}_2 \)

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

<table>
<thead>
<tr>
<th>Component</th>
<th>Approximate Percent by Weight</th>
<th>CAS Number</th>
<th>RTECS Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>5</td>
<td>51-21-8</td>
<td>YR0350000</td>
</tr>
</tbody>
</table>

3. HAZARD INFORMATION

Carcinogen List

<table>
<thead>
<tr>
<th>Substance</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>3</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

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, cardiovascular system, skin and the fetus.

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
Product Name: Fluorouracil Injection, USP

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 known from occupational exposure. 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.

Medical Conditions

Pre-existing hypersensitivity to 5-fluorouracil or other components in this formulation; pre-existing bone marrow, gastrointestinal, nervous system cardiovascular or skin disorders; pregnancy.

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.

Special Fire Fighting Procedures

No special provisions required beyond normal fire fighting 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 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.

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

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>Exposure limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>Not Applicable</td>
<td>N/A</td>
</tr>
</tbody>
</table>

- **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
9. PHYSICAL/CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Liquid</td>
</tr>
<tr>
<td>Color</td>
<td>Sterile, non-pyrogenic injectable solution</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH:</td>
<td>8.6 to 9.4</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point Range:</td>
<td>NA</td>
</tr>
<tr>
<td>Evaporation Rate:</td>
<td>NA</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>NA</td>
</tr>
<tr>
<td>Upper/Lower Flammability or Explosive Limits:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Pressure:</td>
<td>NA</td>
</tr>
<tr>
<td>Vapor Density:</td>
<td>NA</td>
</tr>
<tr>
<td>Specific Gravity:</td>
<td>NA</td>
</tr>
<tr>
<td>Solubility:</td>
<td>NA</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water:</td>
<td>NA</td>
</tr>
<tr>
<td>Auto-ignition temperature:</td>
<td>NA</td>
</tr>
<tr>
<td>Decomposition temperature:</td>
<td>NA</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td>Reactivity</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under recommended storage conditions and use. Active ingredient reported to be light sensitive.</td>
</tr>
<tr>
<td>Hazardous Reactions</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Conditions to avoid</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Incompatibilities</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Hazardous decomposition products</td>
<td>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.</td>
</tr>
<tr>
<td>Hazardous Polymerization</td>
<td>Not anticipated to occur with this product.</td>
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</tbody>
</table>
11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for the ingredients is as follows:

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

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
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.

**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 µg/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.

**Target Organ Effects**

Based on clinical use, possible target organs may include the bone marrow, gastrointestinal system, nervous system, cardiovascular system, skin and the fetus.

### 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.

### 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
Product Name: Fluorouracil Injection, USP

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
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
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
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: This material is not regulated as hazardous material for ground transport under the DOT hazardous materials regulations.

15. REGULATORY INFORMATION

USA Regulations

<table>
<thead>
<tr>
<th>Substance</th>
<th>TSCA Status</th>
<th>CERCLA Status</th>
<th>SARA 302 Status</th>
<th>SARA 313 Status</th>
<th>PROP 65 Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Fluorouracil</td>
<td>Listed</td>
<td>Not Listed</td>
<td>Listed</td>
<td>Listed</td>
<td>Listed</td>
</tr>
</tbody>
</table>

RCRA Status  Not Listed
U.S. OSHA Classification Target Organ Toxin
Reproductive Toxin
Possible Irritant

GHS 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  Not Applicable
Hazard Category  Not Applicable
Signal Word  Not Applicable
Symbol  Not Applicable
Product Name: Fluorouracil Injection, USP

Prevention
P260 - Do not breathe dust/fume/gas/mist/vapors/spray.

Hazard Statement
Not Applicable

Response:
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. Wash hands after handling.

Get medical attention if you feel unwell.

**EU Classification**
*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance 5-Fluorouracil.*

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases:
S23 - Do not breathe vapor.
S24/25 - Avoid contact with skin and eyes.
S37/39 - Wear suitable gloves and eye/face protection.

**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
LD50 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
TSCA Toxic Substance Control Act
TWA 8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS
Date Prepared: 09/22/2011
Obsolete Date: 06/30/2009
Product Name: Fluorouracil Injection, USP

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