

Adrucil® Injection

**1. PRODUCT IDENTIFICATION**

**Product Name** Adrucil® Injection  
**Product Use** Medical Treatment; Antineoplastic  
**Manufacturer Address** Teva Parenteral Medicines, Inc.  
 11 Hughes  
 Irvine, CA 92618-1902

**Chemtrec Emergency No.** 1-800-424-9300 (United States)  
 1-202-483-7617 (International Collect)

**Business Phone** 1-800-729-9991  
**Website Address** <http://www.sicorinc.com>

**Common Names** Fluorouracil Injection

**Chemical Name** 5-fluoro-2,4(1H, 3H)-pyrimidinedione  
**Chemical Formula** C<sub>4</sub>H<sub>3</sub>FN<sub>2</sub>O<sub>2</sub>  
**Chemical Family** Fluorinated Pyrimidine  
**How Supplied** 50 mg/mL in 10 mL vials, 50 mL vials, and 100 mL vials

**Date of Preparation:** June 6, 2003

**2. COMPOSITION AND INGREDIENTS**

CHEMICAL NAME	CAS#	%	EXPOSURE LIMITS IN AIR				
			ACGIH		OSHA		Other
			TLV	CEIL	PEL	CEIL	
Fluorouracil	51-21-8	5	NE	NE	NE	NE	NE
Water (for injection)	7732-18-5	Balance	NE	NE	NE	NE	NE

NE - Not Established                      C - Ceiling Limit  
 NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 – 1998 format  
 CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

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3. HAZARD IDENTIFICATION

**EMERGENCY OVERVIEW:** Material is a clear, light yellow odorless liquid. Harmful if swallowed. Reproductive toxicant. May cause allergic/hypersensitivity reactions. Avoid exposure during pregnancy. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling.

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause mild irritation. Effects may include stinging, watering, and redness of the eyes and redness and a burning sensation on the skin. Skin contact may result in allergic skin reactions.

Ingestion: Although ingestion is not an anticipated route of occupational exposure, this material is toxic if ingested. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, therapeutic effects including changes in the blood and bone marrow; internal bleeding, skin rash, skin or eye, photosensitivity, skin pigment changes, nail changes, loss of nails, tingling, pain, and swelling in the hands and feet, anaphylaxis and generalized allergic reactions, changes in blood pressure, irregular heartbeat, chest pain, and cardiac arrest, disorientation, confusion, and euphoria. See package insert for other adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include mild irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as changes in the blood and bone marrow; internal bleeding, skin rash, skin or eye, photosensitivity, skin pigment changes, nail changes, loss of nails, tingling, pain, and swelling in the hands and feet, anaphylaxis and generalized allergic reactions, changes in blood pressure, irregular heartbeat, chest pain, and cardiac arrest, disorientation, confusion, and euphoria. Possible allergic reaction to material if inhaled, ingested, or in contact with skin.

Cancer: No carcinogenic effects have been reported (see Section 11).

Chronic: Based on animal data, Fluorouracil, the active ingredient, is considered a potential reproductive toxicant (see Section 11).

Target Organs: Potential hazard to the cardiovascular, central nervous, and immune systems (see Section 11).

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**3. HAZARD IDENTIFICATION cont.**

Pre-Existing Medical Conditions: Pre-existing cardiovascular, central nervous, and immune system disorders may be aggravated by exposure to this material.

**4. FIRST-AID MEASURES**

Skin Exposure: Remove contaminated shoes and clothing and cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: If irritation or redness develops, move victim away from exposure and into fresh air. Flush eyes with clean water and seek medical attention.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Victims of chemical exposure must be taken for medical attention. Take a copy of the MSDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians Desk Reference for additional treatment information.

**5. FIRE-FIGHTING MEASURES**

Flash Point: Non-flammable      Autoignition Temperature: Not applicable

Flammable Limits (in air by volume, %): Lower: Not applicable    Upper: Not applicable

Fire Extinguishing Equipment: Use extinguishing agent suitable for type of surrounding fire.

<u>Water Spray:</u> OK	<u>Carbon Dioxide:</u> OK	<u>Halon:</u> OK
<u>Foam:</u> OK	<u>Dry Chemical:</u> OK	<u>Other:</u> Any "ABC" Class

Unusual Fire and Explosion Hazards: No unusual fire or explosion hazards are expected.

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

Special Fire Fighting Procedures.: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.



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### 5. FIRE-FIGHTING MEASURES cont.

NFPA HAZARD CLASS:	Health:	2 (Moderate)
	Flammability:	0 (Least)
	Reactivity:	0 (Least)

### 6. ACCIDENTAL RELEASE MEASURES

#### Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

### 7. HANDLING and STORAGE

**FLUOROURACIL IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.**

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from sources of ignition and any incompatible materials or conditions (see Section 10). Store at room temperature 15-30°C (59-86°F)

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.



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### 8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances 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 warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

### 9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	1	Evaporation Rate (n-BuAc=1):	>1
Specific Gravity (water = 1):	~1	Melting/Freezing Point:	0°C (32°F)
Solubility in Water:	Soluble	Boiling Point:	100°C (212°F)
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	8.6-9.4
Odor Threshold: Odorless			
Appearance and Color: Clear yellow to greenish-yellow solution			

ND = No Data

### 10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility. This product would not be compatible with strong oxidizers, strong acids, and strong bases.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: When heated to decomposition temperatures, or under strongly basic conditions, this product will emit carbon oxides, urea, fluoride, and ammonia.

**11. TOXICOLOGICAL INFORMATION**

Toxicity Data: The following information is for Fluorouracil, the active ingredient

Oral LD50(rat) = 230 mg/kg	IP LD50(rat) = 70 mg/kg	IV LD50(rat) = 245 mg/kg
Oral LD50(mouse) = 115 mg/kg	IP LD50(mouse) = 100 mg/kg	IV LD50(mouse) = 81 mg/kg
Oral LD50(dog) = 30 mg/kg	IM LD50(rat) = 240 mg/kg	IV (LD50(g.pig)) = 25 mg/kg
Oral LD50(rabbit) = 18900 ug/kg	SubQ LD50(rat) = 217 mg/kg	
	SubQ LD50(mouse) = 169 mg/kg	

Suspected Cancer Agent: Adequate long-term studies in animals to evaluate carcinogenic potential have not been conducted with Fluorouracil. It is not listed as carcinogenic by NTP, IARC OSHA.

Irritancy of Product: This product is not expected to be irritating to contaminated skin, eyes and other tissues. The active ingredient is mildly irritating to the eyes and the skin.

Sensitization to the Product: This product may cause allergic type reactions in sensitive individuals.

Target Organ(s): Exposure to this material has not demonstrated classical target organ effects.

Reproductive Toxicity Information: Listed below is information concerning the effects of Fluorouracil on human and animal reproductive systems. This material is classified as a Pregnancy Category D: (Positive evidence of risk)

Mutagenicity: Fluorouracil was not mutagenic in the following assays; Ames bacterial mutation assay, CHO/HGPRT forward mutation assay, mouse micronucleus test, mouse dominant lethal test, rat unscheduled DNA synthesis assay, and the mouse sister chromatid exchange assay. It was positive in the in vitro chromosomal aberration (CHL cell line) and sister chromatid exchange (CHL/IU cell line) assays.

Embryotoxicity/Teratogenicity/Reproductive Toxicity: In a study involving hamsters, all embryos died in utero of animals given either 4.5 mg on gestation day 8-9, or 8 mg on gestation day 10. Defects of development were apparent by gestation day 15 among fetuses from groups treated between gestation days 9-100 with 3 mg of Fluorouracil. No maternal toxicity effects were observed at the embryo-lethal doses.

In a study of Rhesus Monkeys, 8 of 8 animals aborted after treatment with > 40 mg/kg between gestation days 17-27; treatment with 20 mg/kg on gestation days 20-24 caused either fetal absorption or retarded growth.

Fluorouracil has not been adequately studied in animals to permit evaluation of its effects on fertility and general reproductive performance. Additionally, Fluorouracil has not been studied in animals for its effects on peri-and post natal development. Clinical studies on male rats indicate transient infertility as a result of effects on sperm. Fluorouracil has been shown to cross the placenta and enter into the fetal circulation of rats. Studies of female rats, Fluorouracil which is administered in weekly doses of 25-50 mg/kg for 3 weeks during the pre-ovulatory phases of oogenesis, significantly reduced the incidence of fertile matings, delayed the development of embryos, increased the number of pre-implantation lethality, and induced chromosomal abnormalities in embryos.

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

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## 12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: This product will be relatively stable under ambient environmental conditions.

Effect of Materials on Plants or Animals: No specific information is available on the effect of Adrucil on plants or animals in the environment.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect of Adrucil on plants or animals in the aquatic environment.

## 13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" or "characteristic" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

## 14. TRANSPORTATION INFORMATION

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable





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### 15. REGULATORY INFORMATION

#### U.S. REGULATIONS:

U.S. SARA Reporting Requirements: The component Fluorouracil is subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. CERCLA Reportable Quantities (RQ): Not applicable

U.S. TSCA Inventory Status: Adrucil is a “drug” as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product contains Fluorouracil a chemical known to the State of California to cause developmental and reproductive effects.

Other U.S. Federal Regulations: Based on this product’s use, the requirements of the OSHA Bloodborne pathogen Standard (29 CFR 1910.1030) are applicable.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): Harmful if swallowed. Reproductive toxicant. May cause allergic/hypersensitivity reactions. Adrucil should be administered under the supervision of a qualified physician. Avoid over-exposure. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy. Do not eat, drink or smoke when handling Adrucil®. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

#### CANADIAN REGULATIONS:

Canadian DSL/NDSL Status: Adrucil® is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

### 16. OTHER INFORMATION

Issue Date: 06/06/03

Previous Issue Date: None

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