SAFETY DATA SHEET

Product Name: Fludarabine Phosphate for Injection, USP

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Manufacturer Names And Addresses	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA	Hospira Australia Pty Ltd 1 Lexia Place Mulgrave VIC 3170 AUSTRALIA
Emergency Telephone #'s	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	Fludarabine Phosphate for Injection, USP	
Synonyms	9H-Purin-6-amine, 2-fluoro-9-(5-0 -phosphono-β-Darabinofuranosyl) (2-fluoro-ara-AMP); 2-Fluoro-9-(5-O-phosphono-beta-D-arabinofuranosyl)-9H-purin-6-amine.	

2. HAZARD(S) IDENTIFICATION

Emergency Overview

Fludarabine Phosphate for Injection, USP, is a powder containing fludarabine phosphate, a fluorinated nucleotide analog of the anti-viral vidarabine; it acts as a purine antagonist antimetabolite. Clinically, it is used in the treatment of chronic lymphocytic leukemia. It is a cytotoxic agent, and in the workplace, is potentially irritating to the skin, eyes and respiratory tract, a potential occupational reproductive hazard, and potentially harmful to the fetus. Based on clinical use, possible target organs may include the bone marrow, blood, gastrointestinal tract, central nervous system, and lungs.

U.S. OSHA GHS Classification

Physical Hazards	**Hazard Class**	**Hazard Category**
	Not Classified	Not Classified

Health Hazards	**Hazard Class**	**Hazard Category**
	Eye Damage / Irritation	2A
	Skin Corrosion / Irritation	2
	Toxic to Reproduction	2
	Germ Cell Mutagenicity	2
	STOT – RE	2

Label Element(s)

Pictogram

Signal Word

Warning

Hazard Statement(s)

Causes serious eye irritation
Causes skin irritation
Suspected of damaging fertility or the unborn child
Suspected of causing genetic defects
May cause damage to organs through prolonged or repeated exposures

2. HAZARD(S) IDENTIFICATION: continued

Precautionary Statement(s)

Prevention

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

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.

IF ON SKIN (OR HAIR): Wash with plenty of water. Take off contaminated clothing and wash it before reuse. If skin irritation occurs: Get medical advice/attention.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name Fludarabine Phosphate
Chemical Formula $C_{10}H_{13}FN_5O_7P$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Fludarabine Phosphate	50	75607-67-9	UO7440900

Non-hazardous ingredients include mannitol. Hazardous ingredients present at < 1% include sodium hydroxide which is added for pH adjustment.

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 product. However, many organic powders will combust at elevated temperatures.

Fire & Explosion Hazard

None anticipated from this product. Avoid the creation of dusty environments.

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

For powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill control procedures. Collect spilled powder using techniques that minimize powder migration. Clean the affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations.

If a spill occurs after reconstitution, isolate the area around the 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 waste materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Fludarabine phosphate is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastic agents to minimize potential exposures. Several guidelines on handling cytotoxic antineoplastic 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. When handling the powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic 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 antineoplastic 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 allergies to fludarabine phosphate, 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
Fludarabine Phosphate	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.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION: continued

Respiratory Protection	Respiratory protection is normally not needed during intended product use. However, if the generation of dusts or 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 dust or aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. 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 material, 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 oncolytic 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	As a minimum, the use of chemical safety goggles is recommended when handling this material.
Engineering Controls	When handling, local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	A white, lyophilized solid cake
Odor	Odorless
Odor Threshold	NA
pH	7.2-8.2 when reconstituted
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	Water
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 standard use and storage conditions.

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), oxides of phosphorus (POx), and hydrogen fluoride.

Hazardous Polymerization Not anticipated to occur with this product.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity - Information for the product is not available. Information for the active ingredient is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Fludarabine Phosphate	100	LD50	Intravenous	1236	mg/kg	Mouse
Fludarabine Phosphate	100	LD50	Intravenous	910 1050	mg/kg mg/kg	Rat, male Rat, female
Fludarabine Phosphate	100	LD50	Intravenous	1404 1235	mg/kg mg/kg	Mouse, male Mouse, female

LD50 is the dosage producing 50% mortality.

Occupational Exposure Potential There are scientific studies that suggest 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 materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known. Information on the absorption of this product via inhalation or skin contact is not available. Avoid liquid aerosol generation and skin contact.

Signs and Symptoms None anticipated from normal handling of this product. This material should be considered irritating to the skin, eyes, and respiratory tract. In clinical use, adverse effects may include fever, chills, cough, dyspnea, pneumonia, gastrointestinal disturbances, stomatitis, edema, tumor lysis syndrome, skin rashes, auto-immune hemolytic anemia and thrombocytopenia, and hemorrhagic cystitis. Neurological disturbances may include peripheral neuropathy, agitation, confusion, visual disturbances, seizures, and coma. High doses have been associated with progressive encephalopathy, blindness, and death. Bone-marrow suppression may include neutropenia, thrombocytopenia, and anemia. Pulmonary toxicity may include dyspnea, fever, hypoxemia, and interstitial and alveolar infiltration.

Aspiration Hazard None anticipated from normal handling of this product. However, inadvertent inhalation of this product may produce respiratory irritation.

Dermal Irritation/Corrosion None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with itching and redness.

Ocular Irritation/Corrosion None anticipated from normal handling of this product. However, inadvertent eye contact with this product may produce irritation, redness and discomfort.

Dermal or Respiratory Sensitization None anticipated from normal use of this product.

11. TOXICOLOGICAL INFORMATION: continued

Reproductive Effects

None anticipated from normal handling of this product. Studies in mice, rats and dogs have shown dose-related adverse effects on the male reproductive system. A decrease in mean testicular weights in mice and rats with a trend toward decreased testicular weights in dogs, and degeneration and necrosis of spermatogenic epithelium of the testes in mice, rats and dogs were noted.

Fludarabine phosphate was embryolethal and teratogenic in rats and rabbits. Fludarabine phosphate was administered at dosages of 0, 1, 10 or 30 mg/kg/day to pregnant rats on days 6 to 15 of gestation. At 10 and 30 mg/kg/day administered during organogenesis, there was a dose-related increase in various skeletal variations and a decrease in mean fetal body weights. Maternal toxicity was not apparent at 10 mg/kg/day, and was limited to slight body weight decreases at 30 mg/kg/day. In a dose finding study, malformations such as limb and tail defects were induced at a dosage of 40 mg/kg/day (9.6 times the recommended human dose on a mg/m2 basis).

In a reproduction toxicity study on rabbits Fludarabine phosphate was administered intravenously at doses of 0, 1, 5 or 8 mg/kg/day on days 6 to 18 of gestation. A dose of 8 mg/kg/day administered during organogenesis increased embryo and fetal lethality as indicated by a higher number of resorptions and a decrease in live fetuses. Compound-related teratogenic effects manifested by external deformities and skeletal malformations were observed at 8 mg/kg/day. The most frequent external malformations observed in rabbits were cleft palate, adactyly, brachydactyly and syndactyly along with skeletal malformations such as fused metatarsals, phalanges, sternebrae and limb bones and some soft tissue malformations (diaphragmatic herniae). Fetal body weights were decreased in rabbits given 8 mg/kg/day.

Mutagenicity

Fludarabine phosphate was not mutagenic in bacteria (Ames test) or in mammalian cells (HGRPT assay in Chinese hamster ovary cells) either in the presence or absence of metabolic activation. Fludarabine phosphate was clastogenic *in vitro* to Chinese hamster ovary cells (chromosome aberrations in the presence of metabolic activation) and induced sister chromatid exchanges both with and without metabolic activation. In addition, fludarabine phosphate was clastogenic *in vivo* (mouse micronucleus assay) but was not mutagenic to germ cells (dominant lethal test in male mice).

Carcinogenicity

Long-term carcinogenicity studies in animals with fludarabine phosphate have not been conducted.

Carcinogen Lists

IARC: Not listed **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, blood, gastrointestinal tract, central nervous system, and lungs.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product.

Persistence/Biodegradability

Not determined for product.

Bioaccumulation

Not determined for product.

Mobility in Soil

Not determined for product.

Notes:

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	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA
ICAO/IATA STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA
IMDG STATUS	Not regulated
Proper Shipping Name	NA
Hazard Class	NA
UN Number	NA
Packing Group	NA
Reportable Quantity	NA

Notes: DOT - US Department of Transportation Regulations

15. REGULATORY INFORMATION

US TSCA Status	Exempt
US CERCLA Status	Not listed
US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US PROP 65 (Calif.)	Not listed

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
Do not breathe vapor or spray
Wash hands thoroughly after handling
Wear protective gloves/protective clothing/eye protection/face protection

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.

IF ON SKIN (OR HAIR): Wash with plenty of water. Take off contaminated clothing and wash it before reuse. If skin irritation occurs: Get medical advice/attention.

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.

16. OTHER INFORMATION

Notes: NA

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: October 12, 2012
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