MATERIAL SAFETY DATA SHEET

Product Name: Gemcitabine Injection

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

ZHOPL Hospira Oncology Pvt. Ltd.
Plot-3, Pharmez 'Special Economic Zone'
Sarkhej - Bawla highway (NH No 8A), Village: Matada, Tal Sanand
Gujarat, India

Emergency Telephone

CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (61) 290372994

Hospira, Inc., Non-Emergency

224-212-2000

Product Name

Gemcitabine Injection

Synonyms

2′-deoxy-2′,2′-difluorocytidine monohydrochloride (β–isomer); Cytidine, 2'-deoxy-2',2'-difluoro-, monohydrochloride.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name

Gemcitabine Hydrochloride

Chemical Formula

$C_9H_{11}F_2N_3O_4 \cdot HCl$

Preparation

Non-hazardous ingredients include Water for Injection. Hydrochloric acid and/or sodium hydroxide may be added to adjust the pH.

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Gemcitabine Hydrochloride	4.3	122111-03-9	HA3840000

3. HAZARD INFORMATION

Carcinogen List

Substance	IARC	NTP	OSHA
Gemcitabine Hydrochloride	Not Listed	Not Listed	Not Listed

Emergency Overview

Gemcitabine Injection is a solution containing gemcitabine hydrochloride, an analog of cytarabine that inhibits DNA synthesis and induces apoptosis (cell death). Clinically, gemcitabine hydrochloride is used to treat certain types of cancers. In the workplace, this material should be considered irritating to the skin, eyes and respiratory tract, cytotoxic, neurotoxic, and a potential occupational reproductive hazard. Based on clinical use, possible

	target organs include the skin, eyes, nervous system, blood, liver, kidney, and 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 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.
Signs and Symptoms	None known form occupational exposure. In clinical use, adverse effects have included bone marrow suppression (leukopenia, neutropenia, thrombocytopenia, and anemia), nausea, vomiting, diarrhea or constipation, pain, fever, rash, alopecia, stomatitis, dyspnea, hemorrhage, neurotoxicity (mild paresthesias), elevated liver enzymes, and adverse renal effects (proteinuria and hematuria).
Medical Conditions Aggravated by Exposure	Pre-existing hypersensitivity to gemcitabine hydrochloride; pre-existing skin, eye, bone marrow, blood, nervous system, liver, or kidney ailments; 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 from this aqueous product.
Fire & Explosion Hazard	None anticipated from this aqueous product.
Extinguishing media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.

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 liquid with an inert absorbent material (e.g. absorbent pad). Clean affected area with soap and water. Dispose of materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Gemcitabine hydrochloride is a cytotoxic anti-neoplastic 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. If 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 may be 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 gemcitabine hydrochloride, 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	**Type**	**mg/m3**	**ppm**	**µg/m3**	**Note**
Gemcitabine Hydrochloride	Not Applicable	N/A	N/A	N/A	None Established

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. 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 chemotherapy 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

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 also recommended.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	Liquid
Color	Colorless, clear
Odor	Odorless
Odor Threshold:	NA
pH:	NA
Melting point/Freezing point:	NA
Initial Boiling Point/Boiling Point Range:	NA
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	NA
Vapor Pressure:	NA
Vapor Density:	NA
Specific Gravity:	NA
Solubility:	Gemcitabine hydrochloride is soluble in water, slightly soluble in methanol, and practically insoluble in ethanol and polar organic solvents.
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature:	NA
Decomposition temperature:	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), hydrogen chloride 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 ingredients is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
*Gemcitabine Hydrochloride	100	LD50	Oral	>500	mg/kg	Rat
*Gemcitabine Hydrochloride	100	LDLo	Oral	333	mg/kg	Mouse
Gemcitabine Hydrochloride	100	LD50	Intravenous	236	mg/kg	Rat
Gemcitabine Hydrochloride	100	LD50	Intravenous	500	mg/kg	Mouse
*Gemcitabine Hydrochloride	51-53	LD50	Dermal	>1000	mg/kg	Rabbit

*Eli Lilly and Company MSDS

Aspiration Hazard

None anticipated from normal handling of this product.

Dermal Irritation/Corrosion

None anticipated from normal use of this product. However, inadvertent skin contact with this product may produce skin irritation with redness.

Ocular Irritation/Corrosion

None anticipated from normal use of this product. However, inadvertent eye contact with this produce may produce eye irritation with redness and discomfort.

Dermal or Respiratory Sensitization

None anticipated from normal handling of this product. Gemcitabine hydrochloride was negative in a sensitization assay in guinea pigs. Hypersensitivity reactions have been reported infrequently during the clinical use of this product.

Reproductive Effects

Intraperitoneal administration of gemcitabine to male mice at a dosage of 0.5 mg/kg/day produced moderate to severe hypospermatogenesis, decreased fertility, and decreased implantations. In female mice, fertility was not affected but maternal toxicities were noted at intravenous dosages of 1.5 mg/kg/day, and fetotoxicity or embryolethality was observed at an intravenous dosage of 0.25 mg/kg/day. Gemcitabine is embryotoxic, producing fetal malformations (cleft palate, incomplete ossification) at a dosage of 1.5 mg/kg/day in mice. Gemcitabine is fetotoxic causing fetal malformations (fused pulmonary artery, absence of gall bladder) at a dosage of 0.1 mg/kg/day in rabbits. Embryotoxicity is characterized by decreased fetal viability, reduced live litter sizes, and developmental delays.

Mutagenicity

Gemcitabine induced forward mutations *in vitro* in a mouse lymphoma (L5178Y) assay and was clastogenic in an *in vivo* mouse micronucleus assay. Gemcitabine was negative when tested using the Ames, *in vivo* sister chromatid exchange, and *in vitro* chromosomal aberration assays; it did not cause unscheduled DNA synthesis *in vitro*.

Carcinogenicity

Long-term animal studies to evaluate the carcinogenic potential of gemcitabine have not been conducted.

Target Organ Effects

Based on clinical use, possible target organs include the skin, eyes, nervous system, blood, liver, kidney, and fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product. Information for gemcitabine hydrochloride* is as follows:

Rainbow trout 96-hour median lethal concentration: > 1043 mg/L
Fathead minnow 96-hour median lethal concentration: > 1014 mg/L
Daphnia magna 48-hour median effective concentration: > 999 mg/L
Green algae (S. capricornutum) median effective concentration: 5.4 mg/L

(average specific growth rate)
Microorganisms
Fungus (Chaetomium globosum): MIC > 1000 mg/L
Mold (Aspergillus flavus): MIC > 1000 mg/L
Soil bacteria (Comamonas acidovorans): MIC > 1000 mg/L
N-fixing bacteria (Azotobacter chroococcum): MIC > 1000 mg/L
Blue-green algae (Nostoc sp.): MIC 800 mg/L

Persistence/Biodegradability Not determined for product. Information for gemcitabine hydrochloride* is as follows:

Dissociation constant (pKa): 3.58
Kow: 0.053, 0.053, 0.052 (pH 5, 7, 9)
Solubility (g/L): 16.0, 15.3, 15.8 (pH 5, 7, 9)
Light absorption (nm): 268 - 269
Hydrolysis: no significant hydroylsis
Aerobic biodegradation half-life: 30% in 28 days

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 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

IMDG STATUS: Not regulated

ICAO/IATA STATUS: Not regulated

Transport Comments: None

15. REGULATORY INFORMATION

USA Regulations

Substance	TSCA Status	CERCLA Status	SARA 302 Status	SARA 313 Status	PROP 65 Status
Gemcitabine Hydrochloride	Not Listed	Not Listed	Not Listed	Not Listed	Not Listed

RCRA Status Not Listed
U.S. OSHA Classification Target Organ Toxin
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
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 Gemcitabine Hydrochloride

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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: 04/23/2013
Obsolete Date: 10/18/2012

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