MATERIAL SAFETY DATA SHEET

Product Name: Gemcitabine Powder for Solution for Infusion

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

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
	Zydus Hospira Oncology Pvt. Ltd. Plot No.3, 'Pharmez'-Special Economic Zone Sarkhej-Bavia Highway, N.H.No.8-A, Village: Matoda, Tal.Sanand, Dist. Ahmedabad-382 213, Gujarat, India	
Emergency Telephone #'s	CHEMTREC: North America: 800-424-9300; International 1-703-527-3887; Australia (02) 8014 4880	
Hospira, Inc., Non-Emergency	224 212-2055	
Product Name	Gemcitabine Powder for Solution for Infusion	
Synonyms	2′-deoxy-2′,2′-difluorocytidine monohydrochloride (β–isomer); Cytidine, 2'-deoxy-2',2'-difluoro-, monohydrochloride.	

2. HAZARD INFORMATION

Emergency Overview

Gemcitabine Powder for Solution for Infusion is a powder that contains 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 dust or 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

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.

Carcinogen Lists: **IARC:** Not listed **NTP:** Not listed **OSHA:** Not listed

3. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Gemcitabine Hydrochloride
Chemical Formula $C_9H_{11}F_2N_3O_4 \bullet HCl$

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Gemcitabine Hydrochloride	48.5	122111-03-9	HA3840000
Sodium Acetate Trihydrate	3	6131-90-4	AJ4580000

Non-hazardous ingredients include mannitol. Hazardous ingredients present at less than 1% include hydrochloric acid and/or sodium hydroxide which 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 Non-flammable powder. However, powder may be ignitable under high temperature.

Fire & Explosion Hazard None anticipated. As with all powders, minimize the creation of dusty environments.

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 For spilled powder, isolate area around spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Collect the spilled powder using techniques that minimize powder migration. Clean affected area with soap and water. Absorb any liquid with an inert absorbent material (e.g. absorbent pad). Dispose of materials according to the applicable federal, state, or local regulations.

If a spill occurs after reconstitution, absorb liquid with suitable material and 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 controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

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 this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

	Exposure limits			
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**	**Hospira EEL**
Gemcitabine Hydrochloride	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established	8-hr TWA: Not Established
Sodium Acetate Trihydrate	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.
STEL: 15-minute Short Term Exposure Limit.

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.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION: continued

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	White to off-white powder in a vial
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 (Air =1)	NA
Evaporation Rate	NA
Specific Gravity	NA
Solubility	It 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 active ingredient 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
Sodium Acetate	100	LD50	Oral	3530 6891	mg/kg mg/kg	Rat Mouse
Sodium Acetate	100	LD50	Dermal	> 10,000	mg/kg	Rabbit

LD 50: Dosage that produces 50% mortality.
*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.

11. TOXICOLOGICAL INFORMATION: continued

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, and 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.

*Eli Lilly and Company MSDS
Notes:
1. EC50: Concentration in water that produces 50% mortality in Daphnia sp.
2. LC50: Concentration in water that produces 50% mortality in fish.
3. 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

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

U.S. TSCA Status	Exempt.
U.S. CERCLA Status	Not listed
U.S. SARA 302 Status	Not listed
U.S. SARA 313 Status	Not listed
U.S. RCRA Status	Not listed
U.S. 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

U.S. OSHA Classification	Irritant Reproductive Toxin Target Organ Toxin

15. REGULATORY INFORMATION: continued

GHS Classification* *In circumstances where medicinal products are not exempted, the recommended GHS classification for this product is as follows:

Hazard Class	Acute Oral Toxicity	Eye Irritation	Toxic to Reproduction	Mutagenicity	Target Organ Toxicity
Hazard Category	4	2B	2	2	2
Symbol		NA			
Signal Word	Warning	Warning	Warning	Warning	Warning
Hazard Statement	Harmful if swallowed	Causes eye irritation	Suspected of damaging fertility or the unborn child	Suspected of causing genetic defects	May cause damage to the skin, eyes, nervous system, blood, liver, or kidney through prolonged or repeated exposure

Prevention:
Obtain special instructions before use.
Do not eat, drink or smoke when using this product.
Do not handle until all safety precautions have been read and understood.
Use personal protective equipment as required.
Do not breathe dust//mist/vapors/spray.
Wash hands thoroughly after handling.

Response:
IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.
Rinse mouth.
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 advice/attention.
Wash hands after handling.
IF exposed or concerned: Get medical attention/advice.

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.

Classification(s):	Harmful	Irritant	Toxic to Reproduction Category 2	Mutagen Category 2
Symbol:				
Indication of Danger	Xn	Xi	T	T

Risk Phrases:
R21 – Harmful in contact with skin
R22 – Harmful if swallowed
R36/37/38 - Irritating to eyes, respiratory system and skin
R46 – May cause heritable genetic damage
R62 – Possible risk of impaired fertility
R63 – Possible risk of harm to the unborn child

Safety Phrases:
S22: Do not breathe dust
S24: Avoid contact with the skin
S25: Avoid contact with 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
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
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator:	Hospira GEHS
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Disclaimer:

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