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 C₉H₁₁F₂N₃O₄ • HCl

Preparation Non-hazardous ingredients include Water for Injection. Hydrochloric acid and/or 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>Gemcitabine Hydrochloride</td>
<td>4.3</td>
<td>122111-03-9</td>
<td>HA3840000</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>Gemcitabine Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

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 from 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

<table>
<thead>
<tr>
<th>Component</th>
<th>Type</th>
<th>mg/m³</th>
<th>ppm</th>
<th>µg/m³</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine Hydrochloride</td>
<td>Not Applicable</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>None Established</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. 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
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airborne exposures, is also recommended.

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>Colorless, clear</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>NA</td>
</tr>
<tr>
<td>pH</td>
<td>NA</td>
</tr>
<tr>
<td>Melting point/Freezing point</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point</td>
<td>NA</td>
</tr>
<tr>
<td>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</td>
<td>NA</td>
</tr>
<tr>
<td>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>Gemcitabine hydrochloride is soluble in</td>
</tr>
<tr>
<td></td>
<td>water, slightly soluble in methanol, and</td>
</tr>
<tr>
<td></td>
<td>practically insoluble in ethanol and polar</td>
</tr>
<tr>
<td></td>
<td>organic solvents.</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>
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</table>

10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not determined.</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under standard use and storage</td>
</tr>
<tr>
<td></td>
<td>conditions.</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</td>
<td>Not determined. During thermal decomposition,</td>
</tr>
<tr>
<td>products</td>
<td>it may be possible to generate irritating</td>
</tr>
<tr>
<td></td>
<td>vapors and/or toxic fumes of carbon</td>
</tr>
<tr>
<td></td>
<td>oxides (COx), nitrogen oxides (NOx),</td>
</tr>
<tr>
<td></td>
<td>hydrogen chloride and hydrogen fluoride.</td>
</tr>
<tr>
<td>Hazardous Polymerization</td>
<td>Not anticipated to occur with this product.</td>
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</table>

11. TOXICOLOGICAL INFORMATION

Acute Toxicity
Not determined for the product formulation. Information for the ingredients is as follows:
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<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>
</tr>
</thead>
<tbody>
<tr>
<td>*Gemcitabine Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>&gt;500</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>*Gemcitabine Hydrochloride</td>
<td>100</td>
<td>LDL0</td>
<td>Oral</td>
<td>333</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Gemcitabine Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>236</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td>Gemcitabine Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>500</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>*Gemcitabine Hydrochloride</td>
<td>51-53</td>
<td>LD50</td>
<td>Dermal</td>
<td>&gt;1000</td>
<td>mg/kg</td>
<td>Rabbit</td>
</tr>
</tbody>
</table>

*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 product 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
Product Name: Gemcitabine Injection

(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 hydrolysis
- 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

<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>Gemcitabine Hydrochloride</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
<tr>
<td>RCRA Status</td>
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<td></td>
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<tr>
<td>U.S. OSHA Classification</td>
<td>Target Organ Toxin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GHS Classification</td>
<td>Irritant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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:
Product Name: Gemcitabine Injection

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.

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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