Product Name: Irinotecan Hydrochloride 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

Emergency Telephone
CHEMTREC: North America: 800-424-9300;
International 1-703-527-3887; Australia (02) 8014 4880

Hospira, Inc., Non-Emergency 224-212-2000

Product Name
Irinotecan Hydrochloride Injection

Synonyms
(S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo1Hpyrano[3’,4’:6,7]-indolizino[1,2-b]quinolin-9-yl-[1,4’bipiperidine]-1’-carboxylate,
monohydrochloride, trihydrate; (+)-7-Ethyl-10-hydroxycamptothecine 10-[1,4’-
bipiperidine]-1’-carboxylate hydrochloride trihydrate.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name
Irinotecan Hydrochloride Trihydrate

Chemical Formula
C_{33}H_{38}N_{4}O_{6}•HCl•3H_2O

Preparation
Non-hazardous ingredients include Water for Injection, 4.5% sorbitol and 0.09% lactic acid. Hazardous ingredients present at less than 1% are: sodium hydroxide and/or hydrochloric acid, which are 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>Irinotecan Hydrochloride Trihydrate</td>
<td>2</td>
<td>136572-09-3</td>
<td>NA</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>Irinotecan Hydrochloride Trihydrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Emergency Overview

Irinotecan Hydrochloride Injection is a solution containing irinotecan hydrochloride. Clinically, it is used to treat certain types of cancers. It is a cytotoxic agent, and in the workplace, should be considered a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, cardiovascular system, lungs, liver, skin, and the fetus.
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**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.

**Signs and Symptoms**
During occupational use, this material should be considered irritating to the eyes and respiratory tract. In clinical use, adverse effects have included bone marrow suppression, nausea, vomiting, and acute diarrhea. Initially, diarrhea may occur within 24 hours as part of a cholinergic syndrome that can also include sweating, hyper-salivation, abdominal cramps, lachrymation, and miosis. After 24 hours, a more severe, prolonged life-threatening diarrhea can occur. Additional adverse effects may include asthenia, dizziness, anorexia; dermatological reactions such as rashes, alopecia; hepatic effects such as elevations in liver enzymes and bilirubin; pulmonary effects such as interstitial pneumonia and pneumonitis with coughing and dyspnea; and cardiovascular effects such as vasodilation, hypotension, and thromboemolic events. There are also infrequent reports of hypersensitivity reactions.

**Medical Conditions Aggravated by Exposure**
Pre-existing hypersensitivity to irinotecan hydrochloride. Pre-existing bone marrow, blood, cardiovascular, gastrointestinal, central nervous system, pulmonary, liver or skin ailments; or pregnancy.

### 4. FIRST AID MEASURES

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>First Aid Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye contact</td>
<td>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.</td>
</tr>
<tr>
<td>Skin contact</td>
<td>Remove from source of exposure. Flush with copious amounts of water. If irritation occurs or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.</td>
</tr>
<tr>
<td>Inhalation</td>
<td>Remove from source of exposure.</td>
</tr>
<tr>
<td>Ingestion</td>
<td>Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Prophylactic or therapeutic administration of 0.25 to 1 mg of intravenous or subcutaneous atropine may be considered (unless clinically contraindicated) in employees experiencing rhinitis, increased salivation, miosis, lachrymation, diaphoresis, flushing, abdominal cramping, or diarrhea (occurring during or shortly after exposure to irinotecan. These symptoms are expected to occur more frequently with higher irinotecan exposures.</td>
</tr>
</tbody>
</table>

### 5. FIRE FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability</td>
<td>None anticipated for this aqueous product.</td>
</tr>
<tr>
<td>Fire &amp; Explosion Hazard</td>
<td>None anticipated for this aqueous product.</td>
</tr>
<tr>
<td>Extinguishing media</td>
<td>As with any fire, use extinguishing media appropriate for primary cause of fire.</td>
</tr>
<tr>
<td>Special Fire Fighting Procedures</td>
<td>Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.</td>
</tr>
</tbody>
</table>
6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal  Isolate the area around the spill. Put on suitable protective clothing and equipment as specified by site spill procedures. Absorb liquid with suitable material and clean the affected area with soap and water. Application of household bleach for 10 minutes can be used to further clean the affected spill areas. Dispose of all spill materials according to the applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling  Irinotecan hydrochloride, the active ingredient in the formulation, is a cytotoxic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic antineoplastics 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. Upon dilution, photodegradation of irinotecan hydrochloride is accelerated in neutral and alkaline solutions compared with acidic solutions. At pH 10, photodegradation is very rapid while at pH 3, photodegradation is much slower. At pH 7, a 0.34 mg/mL aqueous solution of irinotecan degraded 32% in six hours when exposed to a daylight lamp, and 19% when exposed to a white fluorescent light.

Special Precautions  Persons with known hypersensitivities to irinotecan 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

<table>
<thead>
<tr>
<th>Exposure Guidelines</th>
<th>Exposure limits</th>
<th>Type</th>
<th>mg/m³</th>
<th>ppm</th>
<th>µg/m³</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irinotecan Hydrochloride Trihydrate</td>
<td>Not Applicable</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>None Established</td>
<td></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
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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 this material. 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 this material, 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Appearance/Physical State</td>
<td>Liquid</td>
</tr>
<tr>
<td>Color</td>
<td>Pale yellow, clear</td>
</tr>
<tr>
<td>Odor</td>
<td>NA</td>
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<tr>
<td>Odor Threshold:</td>
<td>NA</td>
</tr>
<tr>
<td>pH</td>
<td>3.5 (3.0 to 3.8)</td>
</tr>
<tr>
<td>Melting point/Freezing point:</td>
<td>NA</td>
</tr>
<tr>
<td>Initial Boiling Point/Boiling Point 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 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>NA</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>
<td>NA</td>
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</tbody>
</table>

10. STABILITY AND REACTIVITY

Reactivity

Not determined.

Chemical Stability

Stable under standard use and storage conditions.

Hazardous Reactions

Not determined.
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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), and hydrogen chloride.

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:

<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>
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</thead>
<tbody>
<tr>
<td>Irinotecan Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>867</td>
<td>mg/kg</td>
<td>Rat</td>
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<tr>
<td></td>
<td>100</td>
<td>LD50</td>
<td>Oral</td>
<td>765-1045</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td>Irinotecan Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>84</td>
<td>mg/kg</td>
<td>Rat</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>132</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>LD50</td>
<td>Intravenous</td>
<td>40</td>
<td>mg/kg</td>
<td>Dog</td>
</tr>
<tr>
<td>Irinotecan Hydrochloride</td>
<td>100</td>
<td>LD50</td>
<td>Intraperitoneal</td>
<td>177</td>
<td>mg/kg</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

Aspiration Hazard
None anticipated from normal handling of this product.

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

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

Dermal or Respiratory Sensitization
None anticipated from normal handling of this product. In clinical use, hypersensitivity reactions have been reported infrequently.

Reproductive Effects
In studies in animals, no significant adverse effects on fertility and general reproductive performance were observed after intravenous administration of irinotecan to rats and rabbits at dosages of up to 6 mg/kg/day. However, in repeat-dose studies, testicular atrophy was noted in rodents at a dosage of 20 mg/kg/day, and in dogs at a dosage of 0.4 mg/kg/day. Intravenous administration to rats and rabbits at a dosage of 6 mg/kg/day during organogenesis produced embryotoxicity characterized by increased post-implantation loss and decreased numbers of live fetuses. Irinotecan was teratogenic in rats at dosages greater than 1.2 mg/kg/day, and in rabbits at a dosage of 6.0 mg/kg/day. Irinotecan administered to rat dams for the period following organogenesis through weaning at dosage of 6 mg/kg/day caused decreased learning ability and decreased female body weights in the offspring.

Mutagenicity
Neither irinotecan nor its major metabolite was mutagenic in the in vitro Ames assay. Irinotecan was clastogenic both in vitro (chromosome aberrations in Chinese hamster ovary cells) and in vivo (micronucleus test in mice).
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Carcinogenicity
Long-term carcinogenicity studies with irinotecan have not been conducted. However, intravenous administration of irinotecan to rats at dosages of 2 mg/kg or 25 mg/kg irinotecan once a week for 13 weeks, followed by recovery for 91 weeks, resulted in a significant dose-related trend for the incidence of combined uterine horn endometrial stromal polyps and endometrial stromal sarcomas.

Target Organ Effects
This product should be considered irritating to the eyes and respiratory tract. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, central nervous system, cardiovascular system, lungs, liver, skin, and the fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity
Not determined.

Persistence/Biodegradability
Not determined.

Bioaccumulation
Not determined.

Mobility in Soil
Not determined.

13. DISPOSAL CONSIDERATIONS

Waste Disposal
All waste materials must be properly characterized. Disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container Handling and Disposal
Dispose of containers 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>
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<tbody>
<tr>
<td>Irinotecan Hydrochloride Trihydrate</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

RCRA Status
Not Listed

U.S. OSHA Classification
Target Organ Toxin
Reproductive Toxin
Possible Irritant
Product Name: Irinotecan Hydrochloride Injection

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
P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P264.1 - Wash hands thoroughly after handling.
P281 - Use personal protective equipment as required.

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 Irinotecan Hydrochloride Trihydrate.

Classification(s): Not Applicable
Symbol: Not Applicable
Indication of Danger: Not Applicable
Risk Phrases: Not Applicable
Safety Phrases: S23 - Do not breathe vapour.
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
Product Name: Irinotecan Hydrochloride Injection

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: 10/11/2011
Obsolete Date: 11/06/2009

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