



## MATERIAL SAFETY DATA SHEET

**Product Name: Irinotecan Hydrochloride Injection**

### 1. CHEMICAL PRODUCT AND COMPANY INFORMATION

<b>Manufacturer Name And Address</b>	Hospira, Inc. 275 North Field Drive Lake Forest, Illinois 60045 USA	Hospira Australia Pty Ltd 1 Lexia Place Mulgrave VIC 3170 AUSTRALIA
<b>Emergency Telephone #'s</b>	CHEMTREC: North America: 800-424-9300; International: 1-703-527-3887; Australia: (02) 8014 4880	
<b>Hospira, Inc., Non-Emergency</b>	224-212-2055	
<b>Product Name</b>	Irinotecan Hydrochloride Injection	
<b>Synonyms</b>	(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-hydroxycamptothecin 10-[1,4'-bipiperidine]-1'-carboxylate hydrochloride trihydrate.	

### 2. HAZARD INFORMATION / CLASSIFICATION

<b>Emergency Overview</b>	Irinotecan Hydrochloride Injection contains 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.		
<b>Occupational Exposure Potential</b>	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.		
<b>Signs and Symptoms</b>	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 thromboembolic events. There are also infrequent reports of hypersensitivity reactions.		
<b>Medical Conditions Aggravated by Exposure</b>	Pre-existing hypersensitivity to irinotecan hydrochloride. Pre-existing bone marrow, blood, cardiovascular, gastrointestinal, central nervous system, pulmonary, liver or skin ailments; or pregnancy.		
<b>Carcinogen Lists:</b>	<b>IARC:</b> Not listed	<b>NTP:</b> Not listed	<b>OSHA:</b> Not listed

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

<b>Ingredient Name</b>	Irinotecan Hydrochloride
<b>Chemical Formula</b>	C <sub>33</sub> H <sub>38</sub> N <sub>4</sub> O <sub>6</sub> •HCl•3H <sub>2</sub> O

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Irinotecan Hydrochloride Trihydrate	2	136572-09-3	NA

Non-hazardous ingredients include water, 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.

#### **4. FIRST AID MEASURES**

<b>Eye Contact</b>	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.
<b>Skin Contact</b>	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.
<b>Inhalation</b>	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, lacrimation, 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.
<b>Ingestion</b>	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

#### **5. FIRE FIGHTING MEASURES**

<b>Flammability</b>	None anticipated for this aqueous product.
<b>Fire &amp; Explosion Hazard</b>	None anticipated for this aqueous product.
<b>Extinguishing Media</b>	As with any fire, use extinguishing media appropriate for primary cause of fire.
<b>Special Fire Fighting Procedures</b>	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**

<b>Spill Cleanup and Disposal</b>	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.
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#### **7. HANDLING AND STORAGE**

<b>Handling</b>	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.
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**7. HANDLING AND STORAGE: continued**

**Handling:** continued      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 USP controlled room temperature storage recommendations noted on the product case label, the primary container label, or the product insert. Do not freeze and protect from light (keep in original outer carton). 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 this material.

**8. EXPOSURE CONTROLS/PERSONAL PROTECTION**

**Exposure Guidelines**

Component	Exposure limits			
	OSHA-PEL	ACGIH-TLV	Hospira EEL	Other Limits
Irinotecan Hydrochloride	8-hr TWA: Not established	8-hr TWA: Not established	8-hr TWA: Not Established	NA

Notes: OSHA PEL: US Occupational Safety and Health Administration – Permissible Exposure Limit  
 ACGIH TLV: American Conference of Governmental Industrial Hygienists – Threshold Limit Value.  
 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 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 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

<b>Appearance/Physical State</b>	A pale yellow, clear, aqueous solution.
<b>Odor</b>	NA
<b>Odor Threshold:</b>	NA
<b>pH:</b>	The pH of the solution is adjusted to 3.5 (range, 3.0 to 3.8).
<b>Melting point/Freezing point:</b>	NA
<b>Initial Boiling Point/Boiling Point Range</b>	Approximately 100°C.
<b>Flash Point:</b>	NA
<b>Evaporation Rate:</b>	NA
<b>Flammability (solid, gas):</b>	NA
<b>Upper/Lower Flammability or Explosive Limits:</b>	NA
<b>Vapor Pressure</b>	NA
<b>Vapor Density (Air =1)</b>	NA
<b>Evaporation Rate</b>	NA
<b>Specific Gravity</b>	NA
<b>Solubility</b>	NA
<b>Partition coefficient: n-octanol/water:</b>	NA
<b>Auto-ignition temperature</b>	NA
<b>Decomposition temperature</b>	NA

## 10. STABILITY AND REACTIVITY

<b>Reactivity</b>	Not determined.
<b>Chemical Stability</b>	Stable under standard use and storage conditions.
<b>Hazardous Reactions</b>	Not determined
<b>Conditions to avoid</b>	Not determined
<b>Incompatibilities</b>	Not determined
<b>Hazardous Decomposition Products</b>	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (CO <sub>x</sub> ), nitrogen oxides (NO <sub>x</sub> ), and hydrogen chloride.
<b>Hazardous Polymerization</b>	Not anticipated to occur with this product.

## 11. TOXICOLOGICAL INFORMATION

### Acute Toxicity

Not determined for the product formulation. Information for the active ingredient, irinotecan hydrochloride, is as follows:

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
Irinotecan Hydrochloride	100	LD50	Oral	867	mg/kg	Rat
	100	LD50	Oral	765-1045	mg/kg	Mouse
Irinotecan Hydrochloride	100	LD50	Intravenous	84	mg/kg	Rat
	100	LD50	Intravenous	132	mg/kg	Mouse
	100	LD50	Intravenous	40	mg/kg	Dog
Irinotecan Hydrochloride	100	LD50	Intraperitoneal	177	mg/kg	Mouse

LD50 is the dosage producing 50% mortality.

**11. TOXICOLOGICAL INFORMATION: continued**

<b>Aspiration Hazard</b>	None anticipated from normal handling of this product.
<b>Dermal Irritation/Corrosion</b>	None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with redness and discomfort.
<b>Ocular Irritation/Corrosion</b>	None anticipated from normal handling of this product. However, inadvertent eye contact of this product with eyes may produce irritation with stinging with redness, watering, and discomfort.
<b>Dermal or Respiratory Sensitization</b>	None anticipated from normal handling of this product. In clinical use, hypersensitivity reactions have been reported infrequently.
<b>Reproductive Effects</b>	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.
<b>Mutagenicity</b>	Neither irinotecan nor its major metabolite was mutagenic in the <i>in vitro</i> Ames assay. Irinotecan was clastogenic both <i>in vitro</i> (chromosome aberrations in Chinese hamster ovary cells) and <i>in vivo</i> (micronucleus test in mice).
<b>Carcinogenicity</b>	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.
<b>Target Organ Effects</b>	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**

<b>Aquatic Toxicity</b>	Not determined.
<b>Persistence/Biodegradability</b>	Not determined.
<b>Bioaccumulation</b>	Not determined.
<b>Mobility in Soil</b>	Not determined.
<b>General Notes</b>	In product stability studies, a solution of irinotecan photodegraded rapidly (about 32% in 6 hours at pH 7.0). Irinotecan is not anticipated to persist in the aquatic environment.

**13. DISPOSAL CONSIDERATIONS**

<b>Waste Disposal</b>	All waste materials must be properly characterized. Disposal should be performed in accordance with the federal, state or local regulatory requirements.
<b>Container Handling and Disposal</b>	Dispose of containers and unused contents in accordance with federal, state and local regulations.

**14. TRANSPORTATION INFORMATION**

<b>DOT STATUS:</b>	Not Regulated
<b>Proper Shipping Name:</b>	NA
<b>Hazard Class:</b>	NA
<b>UN Number:</b>	NA
<b>Packing Group:</b>	NA
<b>Reportable Quantity:</b>	NA

<b>ICAO/IATA STATUS</b>	Not Regulated
<b>Proper Shipping Name:</b>	NA
<b>Hazard Class:</b>	NA
<b>UN Number:</b>	NA
<b>Packing Group:</b>	NA
<b>Reportable Quantity:</b>	NA

<b>IMDG STATUS</b>	Not Regulated
<b>Proper Shipping Name:</b>	NA
<b>Hazard Class:</b>	NA
<b>UN Number:</b>	NA
<b>Packing Group:</b>	NA
<b>Reportable Quantity:</b>	NA

Notes: DOT – US Department of Transportation Regulations

**15. REGULATORY INFORMATION**

<b>U.S. TSCA Status</b>	Exempt
<b>U.S. CERCLA Status</b>	Not listed
<b>U.S. SARA 302 Status</b>	Not listed
<b>U.S. SARA 304 Status</b>	Not listed
<b>U.S. SARA 313 Status</b>	Not listed
<b>U.S. RCRA Status</b>	Not listed
<b>PROP 65 (Calif.)</b>	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

<b><u>U.S. OSHA Classification</u></b>	Possible Irritant Reproductive Toxin Target Organ Toxin
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**15. REGULATORY INFORMATION: continued**

**GHS Classification**

\*Where medicinal products are not exempt, the recommended GHS workplace classification is as follows:

Hazard Class	Acute Oral Toxicity	Eye Irritation	Toxic to Reproduction	Mutagenicity	Target Organ Toxicity
Hazard Category	Not Classified	2B	2	2	2
Symbol	NA	NA			
Signal Word	NA	Warning	Warning	Warning	Warning
Hazard Statement	NA	Causes eye irritation	Suspected of damaging fertility or the unborn child	Suspected of causing genetic defects if ingested.	May cause damage to the bone marrow, gastrointestinal system, central nervous system, cardiovascular system, lungs, liver, and skin through prolonged or repeated exposure.






**GHS Precautionary Statements:**

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

**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.  
 IF exposed or concerned, get medical attention.

**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.

Classification(s):	Harmful	Irritant	Toxic to Reproduction Category 2	Carcinogen Category 3	Mutagen Category 2
Symbol:					
Indication of Danger:	Xn	Xi	T	T	T

**15. REGULATORY INFORMATION: continued**

**EU Classification\*: continued**

<b>Risk Phrases:</b>	R22 – Harmful if swallowed R36/37 - Irritating to eyes and respiratory system R40 - Limited evidence of a carcinogenic effect R46 - May cause heritable genetic damage R60 - May impair fertility R61 - May cause harm to the unborn child R64 - May cause harm to breastfed babies
<b>Safety Phrases:</b>	S23: Do not breathe spray S24: Avoid contact with the skin S25: Avoid contact with eyes S36/37/39 Wear suitable protective clothing, gloves and eye/face protection. S60: This material and its container must be disposed of as hazardous waste

**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 <sub>50</sub>	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:	Global Occupational Toxicology
Date Prepared:	January 14, 2008
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Disclaimer:

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