SAFETY DATA SHEET

IRINOTECAN HYDROCHLORIDE INJECTION

1. SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1. Product Identifier Synonyms	Irinotecan hydrochloride Injection (S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxolHpyrano[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'carboxylatehydrochloride trihydrate; Camptosar; Campto
1.2.Relevant identified uses of the substance or mixture and uses advised against intended use	Antineoplastic
1.3. Details of the supplier of the safety data sheet	Fresenius Kabi Oncology Ltd Echelon Institutional Area, Plot No-11 Sector-32, Gurgaon-122001, Haryana, India Telephone number: +911244885000 Contact E-Mail: nagesh.shrivastava@fresenius-kabi.com
1.4. Emergency Telephone number	+911244885463

2. SECTION 2: HAZARDS IDENTIFICATION

2.1.Classification of substance or mixture

EU Classification

According to Article 1, item 5(a) of CLP Regulation (EC) 1272/2008, medicinal products in finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

GHS Classification	Germ Cell Mutagenicity	Category 2
	Reproductive Toxicity	Category 1B

2.2. Label Elements

Signal Word	Danger
Pictogram	
Hazards Statements	H341 - Suspected of causing genetic defects H360 - May damage fertility or the unborn child
Precautionary Statements	P201 - Obtain special instructions before use P202 - Do not handle until all safety precautions have been read and understood P281 - Use personal protective equipment as required. P308+P313-IF exposed or concerned: Get medical attention/advice P405 - Store locked up P501 - Dispose of contents/container in accordance with all local and national regulations
2.3. Other hazards	No data available for PBT and vPvB or any other hazard

3. SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Not applicable

3.2 Mixtures

Ingredients	Quantity per ml	CAS No	EC No	Index No	Registration No	Classification according to Regulation (EC) No 1272/2008
Irinotecan Hydrochloride Trihydrate	20.0 mg	136572-09-3	-	-	-	AcuteTox.4; Repr.1B; Muta.2 ;H302, H360, H341
Lactic Acid	0.9 mg	50-21-5	200-018-0	-	-	Skin Irrit. 2; Eye Dam. 1; H315, H318
Sorbitol	45.0 mg	50-70-4	200-061-	-	-	Not a hazardous

			5			substance or mixture
Hydrochloric acid	q.s.	7647-01-0	231-595-7	017-002-01-x	01-2119484862-27-xxxx	Met.Corr.1;SkinCo-rr.1B; STOT SE3 ;H290,H314,H335
Sodium Hydroxide	q.s.	1310-73-2	215-185-5	011-002-00-6	01-2119457892-27-xxxx	Met.Corr.1;SkinCorr. 1A; H290, H314
Water for injection	q.s. to 1 mL	7732-18-5	231-791-2	-	-	-

4. SECTION-4 FIRST AID MEASURES

4.1 Description of 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 occurs 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. 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.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 – Hazards Identification and/or Section 11 - Toxicological Information.
Medical Conditions Aggravated by Exposure: None known

4.3. Indication of any immediate medical attention and special treatment needed

Victims of exposure must be taken for medical attention. Take a copy of the SDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians' Desk Reference for additional treatment

information.

5. SECTION 5: FIRE FIGHTING MEASURES

5.1. Extinguishing media

Extinguish fires with CO2, extinguishing powder, foam, or water.
Not recommended extinguishing media: no data available.

5.2. Special hazards arising from the substance or mixture

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.
Fire / Explosion Hazards: Not flammable.

5.3. Advise for fire fighters

During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures

6.1.1. For non-emergency personnel
Avoid contamination with the product.
Notify the effected individuals of the emergency, to be aware of the issues associated.
Avoid contact of the product with skin and eyes.
Remove contaminated clothing and wash before reuse.
6.1.2. For emergency responders
Wear personal protective equipment. Ensure adequate ventilation. Never return spills in original containers for re-use.

6.2. Environmental precautions

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

6.3. Methods and material for containment and cleaning up

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 national, state, or local regulations.

6.4. Reference to other sections

Use the control measures and personal protective equipment described in section 8 of this

SDS. Refer to section 13 of this SDS for disposal considerations.

7. SECTION 7: HANDLING AND STORAGE

7.1. Precautions for safe 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.

7.2. Conditions for safe storage, including any incompatibilities

No special storage 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. Keep away from food, and drink. Advice on Segregation.

7.3. Specific end use(s)

Pharmaceutical product used as Antineoplastic

8. SECTION 8: EXPOSURE CONTROL/PERSONAL PROTECTION

8.1. Control parameters

Exposure Limits

Compound	Issuer	Type	Exposure Limit
Irinotecan hydrochloride Trihydrate	OSHA ACGIH TWA-8 hr ----	PEL TLV OEL STEL	NE NE 2 mcg/m^3 NE
Sorbitol	OSHA ACGIH ----	PEL TLV STEL	NE NE NE
Lactic acid	OSHA ACGIH ----	PEL TLV STEL	NE NE NE

Reference: Safety data Sheet of Sagent Pharmaceuticals, Inc.

8.2. Exposure controls

8.2.1. Appropriate engineering controls

Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limit. It is recommended that all operations be fully enclosed and no air recirculated.

8.2.2. Individual protection measures, such as personal protective equipment

Protective clothing should be selected specifically for the working place, depending on concentration and quantity of the hazardous substances handled.

a) Eye / Face protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

b) 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 oncolytic 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.

c) Respiratory protection: 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.

d) Thermal hazards:

Not applicable

8.2.3. Environmental exposure controls

No data available.

9. SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance/Physical state	Liquid
Odor	NA
Odor threshold	NA
PH	3.1 to 3.7
Melting point/freezing point	NA
Initial boiling point and boiling range	NA
Flash point	NA

Evaporation rate	NA
Flammability (solid, gas)	NA
Upper/lower flammability or explosive limits	NA
Vapor pressure	NA
Vapor density (Air =1)	NA
Relative density	NA
solubility	NA
Partition Coefficient: n-octanol/water	NA
Auto-ignition temperature	NA
Decomposition temperature	NA
Viscosity	NA

10. SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

No data available.

10.2. Chemical stability

Stable at normal temperature and pressures.

10.3. Possibilities of hazardous reactions

Hazardous polymerization will not occur.

10.4. Conditions to avoid

Exposure to light.

10.5. Incompatible materials

As a precautionary measure, keep away from strong oxidizers.

10.6. Hazardous decomposition products

No data available.

11. SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

a) 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
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

Acute Toxicity Comments:

LD50 is the dosage producing 50% mortality.

Acute Toxicity - Reference Material Safety data sheet of Hospira Inc. 275 North Field Drive, Lake Forest, Illinois USA 60045

b) Skin corrosion/irritation	None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce irritation with redness and discomfort.
C) Serious eye damage/irritation	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.
d) Respiratory or skin sensitisation	None anticipated from normal handling of this product. In clinical use, hypersensitivity reactions have been reported infrequently.
e) 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).
f) 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.

g) Reproductive toxicity	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.
h) STOT - single exposure	This product should be considered irritating to the eyes and respiratory tract.
i) STOT - repeated exposure	Not available
j) Aspiration hazard	None anticipated from normal handling of this product.

12. SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

Ecotoxicity: Do not allow product to enter drinking water supplies, wastewater or soil. This product may be harmful to contaminated plant and animal life.

12.2. Persistence and degradability

It is anticipated that this compound will decompose into a variety of organic compounds
Very rapid photodegradation at pH 10.
At pH 3, photodegradation was much slower.
At pH 7, 32% degradation (of a 0.34 mg/mL solution) in 6 hours when exposed to a daylight lamp and 19% degradation when exposed to a white fluorescent lamp at pH 7

12.3. Bioaccumulative potential

No data available

12.4. Mobility in soil

No data available

12.5. Result of PBT and vPvB assessment

No data available

12.6. Other adverse effects

No data available

13. SECTION 13: DISPOSAL CONSIDERATIONS

13.1 Waste treatment method

Waste Disposal	All waste materials must be properly characterized. Further, disposal should be performed in accordance with the national, state or local regulatory requirements.
Container Handling and Disposal	Dispose of container and unused contents in accordance with national, state and local regulations.

14. SECTION 14: TRANSPORT INFORMATION

14.1 UN number

Not available

14.2 UN proper shipping name

Not available

14.3 Transport hazard class(es)

Not available

14.4 Packing group

Not available

14.5 Environmental hazards

Not available

14.6 Special precaution for user

Not available

14.7 Transport in bulk according to Annex II of Marpol and the IBC code

Not available

15. SECTION 15: REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or Mixture

USA Regulations

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

RCRA Status-Not Listed

U.S. OSHA Classification- Target Organ Toxin, Reproductive Toxin and Possible Irritant

15.2 Chemical safety assessment

No Chemical safety assessment has been carried out for the product.

16. SECTION 16: Other information

Sources of data	Information from published literature and Safety Data Sheet of the product Irinotecan Hydrochloride Injection published by Pfizer Inc, Pfizer Pharmaceuticals Group, 235 East 42nd Street, New York, New York 10017.
Abbreviations	**CAS**-Chemical Abstracts Services Number;**CERCLA-** US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; **LD50-** Dosage producing 50% mortality; **NA-** Not applicable/Not available; **OSHA** - US Occupational Safety and Health Administration; **Prop 65-** California Proposition 65; **RCRA-** US EPA, Resource Conservation and Recovery Act; **SARA** - Superfund Amendments and Reauthorization Act; **STOT- SE**- Specific Target Organ Toxicity - Single Exposure; **STOT-RE-** Specific Target Organ Toxicity– Repeated Exposure; **TSCA-** Toxic Substances Control Act; **TWA-** 8-hour Time Weighted Average; **OEL**- Occupational Exposure Limit; **ACGIH**-American Conference of Governmental Industrial Hygienists; **NE**-Not established; **PEL**-Permissible Exposure Limit; **TLV**-Threshold Limit Value; **STEL**-Short Term Exposure Limit
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