MATERIAL SAFETY DATA SHEET

Version No: MSDS/Irino-AUS/DP-006 **Effective Date:** 28th Nov 2022

IRINOTECAN HYDROCHLORIDE CONCENTRATED INJECTION
40 MG/2 ML, 100 MG/5 ML, 300 MG/15 ML and 500 MG/25 ML

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Irinotecan Hydrochloride Concentrated Injection 40 mg/2 mL, 100 mg/5 mL, 300 mg/15 mL and 500 mg/25 mL

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street, Melbourne, VIC, 3000, Australia Telephone: 1800 222 673 (hours 8:30am – 4:30pm)	Intas Pharmaceuticals Ltd. Plot No. 457, 458 Village-Matoda, Bavla Road, Ta. Sanand, Dist. Ahmedabad-382 210, Gujarat, India

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the Substance or Mixture:

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

Label Elements:

Signal Word: Danger

Hazard Statements:
H341 - Suspected of causing genetic defects
H360D - May damage the unborn child

Precautionary Statements:
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

Other Hazards: An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note: This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

SECTION 3 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: Irinotecan Hydrochloride.

Inactive: Sorbitol, Lactic acid, Water for Injections, Sodium hydroxide and Hydrochloric acid.

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Irinotecan Hydrochloride	100286-90-6	Not Listed	Acute Tox.4 (H302) Repr.1B (H360D) Muta.2 (H341)	2%
Sodium hydroxide	1310-73-2	215-185-5	Skin Corr.1A (H314)	**
Lactic acid	50-21-5	200-018-0	Eye Dam. 1 (H318) Skin Irrit. 2 (H315)	*
Hydrochloric acid	7647-01-0	231-595-7	STOT SE 3 (H335) Skin Corr. 1A (H314) Press. Gas Acute Tox. 3 (H331)	**
Sorbitol	50-70-4	200-061-5	Not Listed	*
Water for Injections	7732-18-5	231-791-2	Not Listed	*

Additional Information: * Proprietary ** to adjust pH
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.
In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

SECTION 4 - FIRST AID MEASURES

Description of First Aid Measures:

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

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 3 – Hazards Identification and/or Section 11 - Toxicological Information.

Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed:

Notes to Physician: None

SECTION 5 - FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

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.

Advice for Fire-Fighters: During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

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

Methods and Material for Containment and Cleaning Up:

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

SECTION 7 - HANDLING AND STORAGE

Precautions for Safe Handling: Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Conditions for Safe Storage, Including any Incompatibilities:

Storage Conditions: Store as directed by product packaging.

Specific end use(s): Pharmaceutical product used as Antineoplastic

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters:

Refer to available public information for specific member state Occupational Exposure Limits.

Irinotecan Hydrochloride:
OEL TWA-8 Hr : 2 $\mu g/m^3$

Sodium hydroxide:

ACGIH Ceiling Threshold Limit	:	2 mg/m^3
Australia PEAK	:	2 mg/m^3
Austria OEL – MAKs	:	2 mg/m^3
Bulgaria OEL – TWA	:	2.0 mg/m^3
Czech Republic OEL – TWA	:	1 mg/m^3
Estonia OEL – TWA	:	1 mg/m^3
France OEL – TWA	:	2 mg/m^3
Greece OEL – TWA	:	2 mg/m^3
Hungary OEL – TWA	:	2 mg/m^3
Japan - OELs – Ceilings	:	2 mg/m^3
Latvia OEL – TWA	:	0.5 mg/m^3
OSHA - Final PELS - TWAs	:	2 mg/m^3
Poland OEL – TWA	:	0.5 mg/m^3

Slovakia OEL – TWA	:	2 mg/m^3
Slovenia OEL – TWA	:	2 mg/m^3
Sweden OEL – TWAs	:	1 mg/m^3
Switzerland OEL -TWAs	:	2 mg/m^3

Hydrochloric acid:

ACGIH Ceiling Threshold Limit	:	2 ppm
Australia PEAK	:	5 ppm 7.5 mg/m^3
Austria OEL - MAKs	:	5 ppm 8 mg/m^3
Belgium OEL - TWA	:	5 ppm 8 mg/m^3
Bulgaria OEL - TWA	:	5 ppm 8.0 mg/m^3
Cyprus OEL - TWA	:	5 ppm 8 mg/m^3
Czech Republic OEL - TWA	:	8 mg/m^3
Estonia OEL - TWA	:	5 ppm 8 mg/m^3
Germany - TRGS 900 - TWAs	:	2 ppm 3 mg/m^3
Germany (DFG) - MAK	:	2 ppm 3.0 mg/m^3
Greece OEL - TWA	:	5 ppm 7 mg/m^3
Hungary OEL - TWA	:	8 mg/m^3
Ireland OEL - TWAs	:	5 ppm 8 mg/m^3
Italy OEL - TWA	:	5 ppm 8 mg/m^3
Japan - OELs - Ceilings	:	2 ppm 3.0 mg/m^3
Latvia OEL - TWA	:	5 ppm 8 mg/m^3
Lithuania OEL - TWA	:	5 ppm 8 mg/m^3
Luxembourg OEL - TWA	:	5 ppm 8 mg/m^3
Malta OEL - TWA	:	5 ppm 8 mg/m^3
Netherlands OEL - TWA	:	8 mg/m^3
Poland OEL - TWA	:	5 mg/m^3
Portugal OEL - TWA	:	5 ppm 8 mg/m^3
Romania OEL - TWA	:	5 ppm 8 mg/m^3

Slovakia OEL - TWA	:	5 ppm 8.0 mg/m^3
Slovenia OEL - TWA	:	5 ppm 8 mg/m^3
Spain OEL - TWA	:	5 ppm 7.6 mg/m^3
Switzerland OEL -TWAs	:	2 ppm 3.0 mg/m^3
Vietnam OEL - TWAs	:	5 mg/m^3

Analytical Method: Analytical method available for Irinotecan hydrochloride.

Exposure Controls:

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 limits listed above in this section.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Hands: Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

Eyes: Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin: Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)
Respiratory protection: Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Physical State	:	Aqueous solution
Color	:	Pale yellow

Odor : No data available.
Odor Threshold : No data available.
Molecular Formula : Mixture
Molecular Weight : Mixture
Solvent Solubility : No data available
Water Solubility : No data available
Solubility : Soluble: Water
pH : 3.5
Melting/Freezing Point (°C) : No data available
Boiling Point (°C) : No data available.

Partition Coefficient:
Irinotecan Hydrochloride:

Method	pH	Endpoint	Value
Measured	N/A	Log P	4.37

Lactic acid : No data available
Water for Injection : No data available
Sodium hydroxide : No data available
Hydrochloric acid : No data available
Sorbitol : No data available
Decomposition Temperature (°C) : No data available
Evaporation Rate (Gram/s) : No data available
Vapor Pressure (kPa) : No data available
Vapor Density (g/ml) : No data available
Relative Density : No data available
Viscosity : No data available

Flammablity:
Autoignition Temperature (Solid) (°C) : No data available
Flammability (Solids) : No data available
Flash Point (Liquid) (°C) : No data available
Upper Explosive Limits (Liquid) (% by Vol.) : No data available
Lower Explosive Limits (Liquid) (% by Vol.) : No data available

SECTION 10 - STABILITY AND REACTIVITY

Reactivity: No data available

Chemical Stability: Stable under normal conditions of use.

Possibility of Hazardous Reactions:

Oxidizing Properties: No data available

Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions.

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

Hazardous Decomposition Products: No data available

SECTION 11 - TOXICOLOGY INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Short Term: May be harmful if swallowed. (based on components).

Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on gastrointestinal system. Animal studies have shown a potential to cause adverse effects on the fetus.

Known Clinical Effects: Effects reported during clinical use included vomiting and diarrhea. Effects on blood and blood-forming organs have also occurred. Serious allergic reactions, including anaphylaxis, have been reported.

Acute Toxicity:
Irinotecan Hydrochloride:

Species	Route	End Point	Dose
Rat	Oral	LD 50	867 mg/kg
Rat	Oral	LD 50	1026mg/kg

Lactic acid:

Species	Route	End Point	Dose
Rat	Oral	LD50	3543 mg/kg
Rabbit	Dermal	LD50	> 2000 mg/kg

Sodium hydroxide:

Species	Route	End Point	Dose
Mouse	IP	LD50	40 mg/kg

Hydrochloric acid:

Species	Route	End Point	Dose
Rat	Sub-tenon injection (eye)	LC50 1H	3,124 ppm
Mouse	Inhalation	LC50 1H	1,108ppm
Mouse	Oral	LD50	900mg/kg

Sorbitol:

Species	Route	End Point	Dose
Mouse	Oral	LD50	17,800 mg/kg
Rat	Para-periosteal	LD50	7100mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization:
Irinotecan Hydrochloride:

Study Type	Species	Severity
Eye Irritation	Rabbit	Minimal
Skin Irritation	Rabbit	No effect
Antigenicity- Passive cutaneous anaphylaxis	Mouse	Negative

Lactic acid:

Study Type	Species	Severity
Eye Irritation	Rabbit	Severe
Skin Irritation	Rabbit	Moderate Severe

Sodium hydroxide

Study Type	Species	Severity
Eye Irritation	Rabbit	Severe
Skin Irritation	Rabbit	Severe

Repeated Dose Toxicity:
Irinotecan Hydrochloride

Duration	Species	Route	Dose	End Point	Target Organ
4 Week(s)	Rat	Oral	10 mg/kg/day	LOAEL	Bone marrow, Gastrointestinal System
6 Month(s)	Rat	Intravenous	0.016 mg/kg/day	NOAEL	Blood, Bone Marrow, Male reproductive system
4 Week(s)	Dog	Oral	1 mg/kg/day	NOAEL	Bone Marrow, Gastrointestinal system
26 Week(s)	Dog	Intravenous	0.01 mg/kg/day	NOAEL	Blood

Reproduction & Developmental Toxicity:
Irinotecan Hydrochloride:

Study Type	Species	Route	Dose	End Point	Effect(s)
Embryo / Fetal Development	Rat	Intravenous	6 mg/kg/day	NOAEL	Fetotoxicity
Embryo / Fetal Development	Rabbit	Intravenous	6 mg/kg/day	NOAEL	Fetotoxicity
Prenatal & Postnatal Development	Rat	Intravenous	6 mg/kg/day	LOAEL	Neonatal toxicity
Embryo / Fetal Development	Rat	Intravenous	0.24 mg/kg/day	NOAEL	Teratogenic
Embryo / Fetal Development	Rabbit	Intravenous	0.06 mg/kg/day	NOAEL	Teratogenic

Lactic acid

Study Type	Species	Route	Dose	End Point	Effect(s)
Reproductive & Fertility	Rat	Oral	6.25 mg/kg/day	NOEL	Fertility, Not teratogenic

Genetic Toxicity:
Irinotecan Hydrochloride:

Study Type	Cell Type/Organism	Result
Bacterial Mutagenicity (Ames)	*Salmonella*	Negative
In Vitro Cytogenetics	Chinese Hamster Ovary (CHO) cells	Positive
In Vivo Micronucleus	Mouse	Positive

Carcinogenicity:
Irinotecan Hydrochloride:

Duration	Species	Route	Dose	End Point	Effect(s)
104 Week(s)	Rat	Intravenous	2 mg/kg/week	NOAEL	Not carcinogenic

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Hydrochloric acid:

IARC: Group 3 (Not Classifiable)

SECTION 12 - ENVIRONMENTAL IMPACT INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

Toxicity: No data available

Persistence and Degradability: No data available

Bio-accumulative Potential:

Partition Coefficient:
Irinotecan Hydrochloride:

Method	pH	Endpoint	Value
Measured	N/A	Log P	4.3

Mobility in Soil: No data available

SECTION 13 - DISPOSAL INFORMATION

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

SECTION 14 - TRANSPORTATION INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

SECTION 15 - REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

Irinotecan Hydrochloride:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition65	:	Not Listed
EU EINECS/ELINCS List	:	Not Listed

Sorbitol:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	Present
REACH - Annex IV - Exemptions from the obligations of Register	:	Present
EU EINECS/ELINCS List	:	200-061-5

Sodium hydroxide:

CERCLA/SARA 313 Emission reporting	:	Not Listed
CERCLA/SARA Hazardous Substances and their Reportable Quantities	:	1000 lb 454 kg
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	Present
Standard for the Uniform Scheduling for Drugs and Poisons	:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	:	215-185-5

Lactic acid:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS):	:	Present
EU EINECS/ELINCS List	:	200-018-0

Water for Injection:

CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	Present
REACH - Annex IV - Exemptions from the obligations of Register	:	Present
EU EINECS/ELINCS List	:	231-791-2

Hydrochloric acid:

CERCLA/SARA 313 Emission reporting	:	1.0 %
CERCLA/SARA Hazardous Substances and their Reportable Quantities:	:	5000 lb 2270 kg
CERCLA/SARA - Section 302 Extremely Hazardous TPQs	:	500 lb
CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs	:	5000 lb
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	Present
Standard for the Uniform Scheduling for Drugs and Poisons	:	Schedule 5 Schedule 6
EU EINECS/ELINCS List	:	231-595-7

SECTION 16 - OTHER DATA

Text of CLP/GHS Classification abbreviations mentioned in Section 3
Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed
Acute toxicity, inhalation-Cat.3; H331 - Toxic if inhaled
Skin corrosion/irritation-Cat.1A; H314 - Causes severe skin burns and eye damage
Serious eye damage/eye irritation-Cat.1; H318 - Causes serious eye damage
Skin corrosion/irritation-Cat.2; H315 - Causes skin irritation
Specific target organ toxicity, single exposure; Respiratory tract irritation-Cat.3; H335 - May cause respiratory irritation

Data Sources: Information from published literature.

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