MATERIAL SAFETY DATA SHEET

Version No: MSDS/Topo-AUS/DP-001 **Effective Date:** 09th December 2019

Topotecan hydrochloride Concentrated Injection 1 mg/mL, 1 mL and 4 mL

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Topotecan hydrochloride Concentrated Injection 1 mg/mL, 1 mL and 4 mL

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street, Melbourne, VIC, 3000, Australia	Intas Pharmaceuticals Ltd. Plot No. 457, 458 Sarkhej-Bavla Highway, Matoda, Tal. Sanand, Dist. Ahmedabad- 382210, Gujarat, India

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: Topotecan hydrochloride

Inactive: Tartaric acid powder, Sodium hydroxide, Hydrochloric acid and Water for injections.

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Topotecan hydrochloride	119413-54-6	Not Listed	Repr. 1B (H361D) 1B (H340)	0.1
Tartaric acid	87-69-4	201-766-0	Not Listed	*
Sodium hydroxide	1310-73-2	215-185-5	Skin Corr.1A (H314)	**
Hydrochloric Acid	7647-01-0	231-595-7	STOT SE 3 (H335) Skin Corr. 1A (H314) Press. Gas Acute Tox. 3 (H331)	**
Water for injection	7732-18-5	231-791-2	Not Listed	*

* 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 3 - HAZARDS IDENTIFICATION

Classification of the Substance or Mixture:

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

Label Elements

Signal Word: Danger

Hazard Statements:
H361 - Suspected of damaging fertility or the unborn child
H340 - May cause genetic defects

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

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 4 - EMERGENCY & 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: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters: During all fire fighting 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 spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. 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: Designate a change area to facilitate 'good laboratory' decontamination practices. Restrict access to work area. Ground and bond all bulk transfer equipment. No open handling permitted. All operations should be fully enclosed. Avoid inhalation and contact with skin, eye, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash hands and any exposed skin after removal of PPE. 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 drug product Antineoplastic

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

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

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

Sodium hydroxide:

ACGIH Ceiling Threshold Limit	:	2 mg/m3
Australia PEAK	:	2 mg/m3
Austria OEL – MAKs	:	2 mg/m3

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

Tartaric acid:
Germany (DFG) – MAK : 2 mg/m^3

Topotecan hydrochloride:
Occupational Exposure Band (OEB) : OEB 5 (control exposure to <1µg/m^3)

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. It is recommended that all operations be fully enclosed and no air recirculated.

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	:	Lyophilized powder
Color	:	Light yellow to Green
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
pH	:	2.6-3.2
Melting/Freezing Point (°C)	:	No data available
Boiling Point (°C)	:	No data available

Partition Coefficient:

Tartaric acid	:	No data available
Water for injection	:	No data available
Sodium hydroxide	:	No data available
Hydrochloric Acid	:	No data available
Topotecan hydrochloride	:	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: Accidental ingestion may cause effects similar to those seen in clinical use.

Known Clinical Effects: Adverse effects associated with therapeutic use include decreased white blood cells (leukopenia), gastrointestinal disturbances, diarrhea, fever, vasodilation, liver enzyme changes, fatigue, weakness, loss of hair, hypersensitivity reactions.

Acute Toxicity:

Sodium hydroxide:

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

Irritation / Sensitization:

Sodium hydroxide:

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

Reproduction & Development Toxicity:

Topotecan hydrochloride:

Duration	Species	Route	Dose	End Point	Effect(s)
Embryo / Fetal Development	Rabbit	Intravenous	0.1 mg/kg/day	LOAEL	Maternal toxicity, Embryotoxicity, Fetotoxicity
Embryo / Fetal Development	Rat	Intravenous	0.23 mg/kg/day	LOAEL	Fetotoxicity

Genetic Toxicity:

Topotecan hydrochloride:

Study Type	Cell Type/Organism	Result
In Vitro Mammalian Cell Mutagenicity	Human Lymphocytes	Positive
In Vitro Mammalian Cell Mutagenicity	Mouse Lymphoma	Positive
In Vivo	Mouse Bone Marrow	Positive

Carcinogen Status: Not listed as a carcinogen by IARC, NTP or US OSHA.

Hydrochloric Acid IARC: Group 3 (Not Classifiable)

SECTION 12 - ENVIRONMENTAL IMPACT INFORMATION

Environmental Overview: Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

Toxicity:

Aquatic Toxicity:

Topotecan hydrochloride:

Species	End Point	Duration	Result
Daphnia magna (Water Flea)	EC50	48 Hours	61.8 mg/L
Pimephales promelas (Fathead Minnow)	EC50	96 Hours	45.7 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential: No data available

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

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
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
Tartaric acid:		
CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	Not Listed
Inventory - United States TSCA - Sect. 8(b)	:	Present
Australia (AICS)	:	201-766-0
EU EINECS/ELINCS List	:	Present

Topotecan hydrochloride:		
CERCLA/SARA 313 Emission reporting	:	Not Listed
California Proposition 65	:	Not Listed
EU EINECS/ELINCS List	:	Not Listed
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

SECTION 16 - OTHER DATA

Text of CLP/GHS Classification abbreviations mentioned in Section 3
Skin corrosion/irritation-Cat.1A; H314 - Causes severe skin burns and eye damage
Germ cell mutagenicity-Cat.1B; H340 - May cause genetic defects
Reproductive toxicity-Cat.1B; H361 - Suspected of damaging fertility or the unborn child
Specific target organ toxicity, single exposure; Respiratory tract irritation-Cat.3; H335 - May cause respiratory irritation
Acute toxicity, inhalation-Cat.3; H331 - Toxic if inhaled

Data Sources: Information from published literature.

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