Material Safety Data Sheet

SECTION 1. PRODUCT IDENTIFICATION

Product Name	Topotecan Hydrochloride for Injection (4 mg /vial, 5mL vial)
Manufacturer's Name:	Sun Pharmaceutical Industries Limited
Address	Sun Pharmaceutical Industries Ltd. Acme Plaza, Andheri-Kurla Road, Andheri (E) Mumbai – 400 059, INDIA
Trade names:	Topotecan Hydrochloride for Injection

Note: This MSDS is written to provide health and safety information for personnel that will be handling the final product (i.e. transportation, distribution and health care workers).

SECTION 2. COMPOSITION AND INGREDIENTS

COMPONENT	CAS#	FORMULA	PERCENT
Topotecan HCl	119413-54-6	$C_{23}H_{23}N_3O_5$•HCl	5.5%
Mannitol (Pyrogen free), USP	69-65-8	$(C_6H_8(OH)_6)$	66.7%
Tartaric Acid, USP	87-69-4	$C_4H_6O_6$	27.8%

SECTION 3. HAZARDS IDENTIFICATION

Fire and Explosion	This product is classified as non-flammable.
Health	Exposure might occur via skin; eyes; ingestion. Caution - Potent pharmaceutical agent. May cause cancer. May produce adverse effects on the development of human offspring. Possible effects of overexposure in the workplace include: nausea; vomiting; diarrhea; bone marrow toxicity. Health effects information is based on hazards of components.
Environment	No information is available about the potential of this product to produce

adverse environmental effects.

SECTION 4. FIRST-AID MEASURES

Ingestion Never attempt to induce vomiting. Do not attempt to give any solid or liquid by mouth if the exposed subject is unconscious or semi-conscious. Wash out the mouth with water. If the exposed subject is fully conscious, give plenty of water to drink. Obtain medical attention.

Inhalation Physical form suggests that risk of inhalation exposure is negligible.

Skin Contact Using appropriate personal protective equipment, remove contaminated clothing and flush exposed area with large amounts of water. Obtain medical attention if skin reaction occurs, which may be immediate or delayed.

Eye Contact Wash immediately with clean and gently flowing water. Continue for at least 15 minutes. Obtain medical attention.

NOTES TO HEALTH PROFESSIONALS

Medical Treatment Medical treatment in cases of overexposure should be treated as an overdose of a cytotoxic agent.

Medical Conditions Caused or Aggravated by Exposure None for occupational exposure.

Health Surveillance Procedures The need for pre-placement and periodic health surveillance must be determined by risk assessment. Following assessment, if the risk of exposure is considered significant then exposed individuals should undergo appropriate health surveillance that may include symptom enquiry, clinical examination and monitoring of lead organ effects (e.g. full blood counts). In the event of overexposure, individuals should receive post exposure health surveillance focused on the most likely health effects (e.g. full blood counts).

Antidotes No specific antidotes are recommended.

SECTION 5. FIRE-FIGHTING MEASURES

Fire and Explosion Hazards Not expected for the product, although the packaging is combustible.

Extinguishing Media Water is recommended for fires involving packaging.

Special Firefighting Procedures For single units (packages): No special requirements needed. For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapors might be evolved from fires involving this product and associated packaging, self-contained breathing apparatus and full protective equipment are recommended for firefighters. If possible, contain and collect

firefighting water for later disposal.

Hazardous Combustion Products Toxic, corrosive or flammable thermal decomposition products are expected when the product is exposed to fire.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal Precautions For all spills, isolate the spill area, restrict access, post the area for a carcinogen and immediately implement emergency procedures for cleanup and control of occupational carcinogens. Wear protective clothing and equipment consistent with the degree of hazard.

Environmental Precautions Do not allow this material to enter surface drainage systems, sewers and poorly ventilated areas.

Clean-up Methods Spread an inert absorbent on the spill and place in a suitable, properly labeled container for recovery or disposal.

Decontamination Procedures Surfaces should be decontaminated so that potential exposures do not exceed the hygiene guide specified in Section 8 of this SDS. The pH of the collected wash waters should be adjusted using base, such as sodium hydroxide, to a pH greater than 8; commercial bleach solution, containing approximately 5% hypochlorite, should then be added to the waste water. Microgram levels of surface contamination can be using ultraviolet light.

SECTION 7. HANDLING AND STORAGE

HANDLING

General Requirements Isolation or enclosure is recommended to control exposure to this material.

STORAGE The recommended temperature for storage is 15-30°C.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

INGREDIENT	TOPOTECAN	
Occupational Hazard Category	4	
Occupational Exposure Limit	0.03 MCG/M3 (8 HR TWA)	CARCINOGEN, REPRODUCTIVE HAZARD, HIGHLY POTENT

ENGINEERING CONTROLS

Containment	Open handling may result in overexposure. Consider use of enclosures.
Administrative	Entry to the working area should be controlled.

PERSONAL PROTECTIVE EQUIPMENT

Eye Protection	Wear approved safety glasses with side shields if eye contact is possible.
Gloves	The selection of gloves for a specific activity must be based on the material's properties and on possible permeation and degradation that may occur under the circumstances of use. Glove selection must take into account any solvents and other hazards present. Potential allergic reactions can occur with certain glove materials (e.g. Latex) and therefore these should be avoided. Care must be exercised if no data are available and further guidance should be sought from your local safety department. Glove selection must take into account any solvents and other hazards present.
Respirators	Respiratory protective equipment (RPE) is not required for normal handling of this material.
Other Equipment or Procedures	Wear appropriate clothing to avoid skin contact.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	
Physical Form	Lyophilized powder.
pH of Aqueous Solutions	3

SECTION 10. STABILITY AND REACTIVITY

Stability	This product is expected to be stable.
Conditions to Avoid	None for normal handling of this product.

SECTION 11. TOXICOLOGICAL INFORMATION

Oral Toxicity	Toxicity might occur following ingestion.
Inhalation Toxicity	No studies have been conducted.
Skin Effects	Irritation is not expected following direct contact.
Eye Effects	Irritation is not expected following direct contact with eyes.
Target Organ Effects	Adverse effects might occur in the following organ(s) following overexposure: bone marrow and formation of blood cells.
Sensitization	Potential for inducing allergic reactions via the dermal or respiratory route is not known.
Genetic Toxicity	Known or probable human mutagen.

Carcinogenicity Contains a component listed as a carcinogen by: (SUN). No components are listed as carcinogens by: (IARC); (NTP); (US OSHA).

Reproductive Effects Contains components which have been classified as: Known or presumed to cause toxicity in developing human offspring. Known or presumed to impair fertility in human females.

Pharmacological Effects This preparation contains ingredient(s) with the following activity: a cytotoxic agent.

Other Adverse Effects Overexposure in the workplace might have the following effects: reduced white blood cell count; nausea; diarrhea; vomiting; fatigue.

SECTION 12. ECOLOGICAL INFORMATION

Summary No information is available about the potential of this product to produce adverse environmental effects. This material contains an active pharmaceutical ingredient that has been tested and which may be harmful if released directly to the environment. Consult the MSDS of the active ingredient for specific information about potential environmental effects. Appropriate precautions should be taken to limit release of this material to the environment. Local regulations and procedures should be consulted prior to environmental release.

Specific information on the active pharmaceutical ingredient is provided below.

ECOTOXICITY

Aquatic

Microtox Microtox is a general toxicity test which utilizes a sensitive marine photo bacteria as the test species. This material contains an active pharmaceutical ingredient that is not toxic to these microorganisms.

EC50: 102 mg/L, 15 Minutes

Daphnid This material contains an active pharmaceutical ingredient that is harmful to daphids.

EC50: 61.8 mg/L, 48 Hours, Daphnia magna, Static test

Fish This material contains an active pharmaceutical ingredient that is harmful to fish.

Adult Pimephales promelas, fathead minnow

EC50: 45.7 mg/L, 96 Hours, Static test

Adult Pimephales promelas, fathead minnow

NOEL: 25 mg/L, 96 Hours, Static test

MOBILITY

Solubility This material contains an active pharmaceutical ingredient that for environmental fate predictions has solubility in water.

Adsorption This material contains an active pharmaceutical ingredient that is not likely to adsorb to sludge or biomass if released directly to the environment.

Sludge Biomass Distribution Coefficient (log Kd): 2.28 Measured

Partitioning This material contains an active pharmaceutical ingredient with octanol/water partition coefficient data that suggests that for environmental fate predictions the active pharmaceutical ingredient will not have the tendency to distribute into fats.

PERSISTENCE/DEGRADATION

Hydrolysis This material contains an active pharmaceutical ingredient that has been shown to be chemically stable in water. Hydrolysis is unlikely to be a significant depletion mechanism.

Half-Life, Neutral: 35 Years, Measured

Photolysis This material contains an active pharmaceutical ingredient that has been shown to be chemically unstable in water when exposed to light. Aqueous photolysis may be a significant depletion mechanism.

Half-Life, Aqueous: 2.51 Minutes, Measured

Biodegradation This material contains an active pharmaceutical ingredient that is not readily biodegradable (as defined by 1993 OECD Testing Guidelines).

Aerobic - Ready

Percent Degradation: 0 %, 28 days, Batch activated sludge (BAS), Residential sludge

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal Recommendations Collect for recycling or recovery if possible. The disposal method for rejected products/returned goods must ensure that they cannot be re-sold or re-used. The recommended method of disposal is incineration.

Regulatory Requirements Observe all local and national regulations when disposing of this product.

SECTION 14. TRANSPORT INFORMATION

The SDS should accompany all shipments for reference in the event of spillage or accidental release. Only authorized persons trained and competent in accordance with appropriate national and international regulatory requirements may prepare dangerous goods for transport.

UN Classification and Labelling

Technical Name	Topotecan Hydrochloride for Injection
Material	Medicine, solid, toxic, nos (Topotecan Hydrochloride for Injection)
UN Number	UN 3249
Class/Division	6.1
Packing Group	III
Risk Label(s)	Class 6.1 Toxic

International Air Transport (IATA Requirements)

UN/ID Number	ID 8000
Proper Shipping Name/Description	Consumer Commodity
ICAO/IATA Class/Division	9
Subsidiary Risk	None
Packing Group	Not applicable (use packing instruction 910).
Hazard Label(s)	Class 9

Limited Quantities	Quantities equal to or less than 0.5 kg per inner packaging are not subject to the full packaging and labeling requirements, although the appropriate shipping papers will be required.

International Maritime Transport (IMDG Requirements)

UN Number	UN 3249
Material Name/Description	Medicine, solid, toxic, nos
IMO Class/Division	6.1
Subsidiary Risk	None
Packing Group	III
Class Label(s)	Class 6.1 Toxic

Marine Pollutant Status	Not listed
Limited Quantities	Quantities equal to or less than 3 kg per inner packaging are not subject to the full packaging and labeling requirements, although the appropriate shipping papers will be required.

US Domestic Transport (DOT Requirements)

Proper Shipping Name	Consumer Commodity, ORM-D
DOT Hazard Class/Division	ORM-D
UN/NA Number	Not applicable.
Packing Group	Not applicable
US Emergency Response Guide Number	151
Quantity Limitations	Quantities equal to or less than 0.25 kg per inner packaging are not subject to the full packaging and labeling requirements, although the appropriate shipping papers will be required.

European Ground Transport (ADR/RID Requirements)

Classification and Labeling	Not subject to ADR, see SP 601.

SECTION 15. REGULATORY INFORMATION

The information included below is an overview of the major regulatory requirements. It should not be considered to be an exhaustive summary. Local regulations should be consulted for additional requirements.

EU Classification and Labeling

Exempt from requirements of EU Dangerous Preparations directive - product regulated as a medicinal product, cosmetic product or medical device.

Safety Phrase(s)

S23 - Do not breathe .
S25 - Avoid contact with eyes.
S26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S29 - Do not empty into drains.
S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.
S38 - In case of insufficient ventilation, wear suitable respiratory equipment.
S53 - Avoid exposure - obtain special instructions before use.
S60 - This material and/or its container must be disposed of as hazardous waste.

US OSHA Standard (29 CFR Part 1910.1200)

Classification This product is classified as hazardous according to the OSHA Hazard Communication Standard.

Other US Regulations

TSCA Status Exempt

SECTION 16. OTHER INFORMATION

SDS Sections Updated

Sections	Subsections
ECOLOGICAL INFORMATION	Activated Sludge Respiration
	Adsorption
	Algal
	Algal Degradation
	Bioaccumulation
	Biodegradation
	Daphnid

Distribution
Earthworm
Ecotoxicity
Fish
Hydrolysis
Microbial Growth Inhibition
Microtox
Mobility
Other Adverse Effects
Other Species - Aquatic
Other Species - Terrestrial
Partitioning
Persistence/Degradation
Photolysis
Solubility
Summary
Volatility

REGULATORY INFORMATION
TRANSPORT INFORMATION

To the best of our knowledge, the information contained in this material safety data sheet is accurate. However, Sun Pharmaceutical Industries Ltd. does not assume any liability whatsoever for the accuracy or completeness of the information contained herein except for the product's use as intended. Final determination of the suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards, which exist.