

PART I *What is the material and what do I need to know in an emergency?*

1. PRODUCT IDENTIFICATION

PRODUCT NAME (AS LABELED): **TOPOSAR®**

SUPPLIER/MANUFACTURER'S NAME: **Sicor Pharmaceuticals, Inc.**

ADDRESS: 19 Hughes
Irvine, CA 92618

CHEMTREC EMERGENCY NO.: 1-800-424-9300 (United States)**
1-202-483-7616 (International Collect)

BUSINESS PHONE: 1-800-729-9991

FAX: 1-949-855-821

Common Names: Etoposide, VP-16-213, VePesid7
 Chemical Name: 4-demethylepipodophyllotoxin 9-[4,6-0-(R)-ethylidene-b-D-glucopyranoside
 Chemical Formula: C₂₉H₃₂O₁₃
 Chemical Family: Podophyllotoxin, antineoplastic agent
 How Supplied: 20 mg/mL solution in 6 mL, 30 mL and 50 mL vials

2. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	% by weight	EXPOSURE LIMITS IN AIR					
			ACGIH		OSHA			OTHER
			TLV ppm	STEL ppm	PEL ppm	STEL ppm	IDLH ppm	
ETOPOSIDE	33419-42-0	1.96	NE	NE	NE	NE	NE	---
POLYETHYLENE GLYCOL 300, NF	25322-68-3	63.6	NE	NE	NE	NE	NE	---
DEHYDRATED ETHANOL, USP	64-17-5	23.4	1000	NE	1000	NE	NE	---
POLYSORBATE 80, NF	9005-65-6	7.8	NE	NE	NE	NE	NE	---
BENZYL ALCOHOL, NF	100-51-6	3.0	NE	NE	NE	NE	NE	---
CITRIC ACID, anhydrous, NF	77-92-9	0.2	NE	NE	NE	NE	NE	---

* NE = Not Established. **Chemtrec number: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this chemical.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: This material is a flammable liquid, which is also toxic by ingestion or injection.

SYMPTOMS OF OVER EXPOSURE BY ROUTE OF EXPOSURE: This material may be harmful if swallowed, or injected into skin. Various gastrointestinal and allergic reactions have been reported. Injection may lead to a sudden drop in blood pressure.

INHALATION: Inhalation of this product may cause symptoms similar to those caused by ingestion or injection.

CONTACT WITH SKIN or EYES: Contact of the product with the skin or eyes may cause irritation or a local allergic reaction.

SKIN ABSORPTION: There is currently no evidence that skin absorption is a significant route of entry for this product.

INGESTION: Studies indicate that this product IS toxic by ingestion. Nausea and vomiting may occur after ingestion of therapeutic doses; acute ingestion may result in severe gastrointestinal distress.

INJECTION: Injection of this product can lead to bone marrow suppression and associated loss of blood cells, gastrointestinal problems, sudden and severe loss of blood pressure, allergic reactions characterized by chills, fever, cardiac irregularities, and breathing difficulty. Other symptoms of exposure include loss of hair, after-taste, vision difficulty, and liver disorders.

HEALTH EFFECTS OR RISKS FROM EXPOSURE (An explanation in *lay terms*).

ACUTE: Acute exposure generally results in nausea, vomiting, and a loss of blood pressure. Such acute exposure may be life-threatening.

CHRONIC: Chronic exposure to this product may result in cancer, fetal toxicity, teratogenic and mutagenic effects, hair loss, and abnormal skin pigmentation.

HAZARDOUS MATERIAL INFORMATION SYSTEM			
HEALTH		(BLUE)	3
FLAMMABILITY		(RED)	3
REACTIVITY		(YELLOW)	0
PROTECTIVE EQUIPMENT			X
EYES	RESPIRATORY	HANDS	BODY
See Section 8 of this MSDS.			
PPE used during medical treatment of cancer.			

PART II *What should I do if a hazardous situation occurs?*

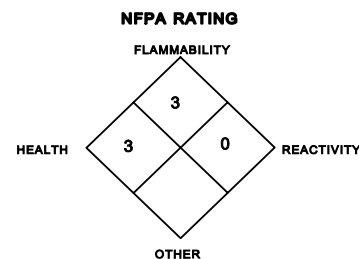
4. FIRST-AID MEASURES

If spilled on skin, immediately wash the affected area with soap and water and rinse with running water for at least 15 minutes. Remove exposed or contaminated clothing, taking care not to contaminate eyes. If the product is splashed in eyes, open victim's eyes while under gentle running water. Use sufficient force to open eye lids. Have victim "roll" eyes. Minimum flushing should be 15 minutes. If the product is inhaled, remove victim to fresh air and use artificial respiration to support vital functions. Remove or cover gross contamination to avoid exposure to rescuers. Victim and rescuers should obtain medical attention, if appropriate.

If the product is swallowed, rinse victim=s mouth and CALL a PHYSICIAN OR a POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, DO NOT induce vomiting. Victim(s) of contamination with this product and all rescuers should be taken for medical attention, if appropriate. Take copy of label and MSDS to physician or health professional with victim. If this material is injected, treat victim for symptoms. No proven antidotes for this drug are known.

5. FIRE-FIGHTING MEASURES

FLASH POINT, EC (method): 15°C-21°C
AUTOIGNITION TEMPERATURE, EC: Not determined
FLAMMABLE LIMITS (in air by volume, %): Lower: 3.3
Upper: 24.5



FIRE EXTINGUISHING MATERIALS: The size and nature of this product is such that it will not contribute to the intensity of a fire. Fire fighting should be aimed at surrounding materials.

Water Spray: OK Carbon Dioxide: OK
Foam: OK Dry Chemical: OK Halon: OK

SPECIAL FIRE FIGHTING PROCEDURES: Incipient fire responders should wear eye protection. Structural fire fighters must wear self-contained breathing apparatus and full protective equipment.

UNUSUAL FIRE and EXPLOSION HAZARDS: When heated to decomposition, this product may emit toxic fumes.

6. ACCIDENTAL RELEASE MEASURES

SPILL and LEAK RESPONSE: For small releases of this product wear latex or nitrile gloves and safety glasses. Large or uncontrolled releases should be responded to by trained personnel using pre-planned procedures. Proper protective equipment should be used. Respiratory protection should be used. Absorb spilled liquid with polypads or other appropriate materials. Avoid splashing or spraying liquid. Rinse area thoroughly with soap and water. Place all spill residue in a double plastic bag. Dispose of in accordance with Federal, State, and local waste disposal regulations.

PART III *How can I prevent hazardous situations from occurring?*

7. HANDLING and STORAGE

WORK PRACTICES and HYGIENE PRACTICES: As with all chemicals, avoid getting this material ON YOU or IN YOU. Wash hands after handling this product. Do not eat or drink while handling this product. Wash hands thoroughly after handling this product or equipment and containers which contain this product. Follow SPECIFIC USE INSTRUCTIONS supplied with product.

STORAGE and HANDLING PRACTICES: Store product in original container at 15 - 30°C.

PROTECTIVE PRACTICES DURING MAINTENANCE OF CONTAMINATED EQUIPMENT: When cleaning non-disposable equipment, wear gloves (double-gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials, and other disposable items contaminated with this product should be disposed of properly.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

VENTILATION and ENGINEERING CONTROLS: Use with adequate ventilation. Follow standard medical product handling procedures.

RESPIRATORY PROTECTION: None required under routine conditions of use.

EYE PROTECTION: Safety glasses.

HAND PROTECTION: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands after removing gloves.

BODY PROTECTION: Routine medical clothing, such as lab coat, gown, or smock, should be worn when preparing or handling this product.

Product Preparation Instructions for Medical Personnel: As with other potentially toxic compounds, care should be practiced in handling and preparing solutions of Etoposide. The use of gloves is recommended. If Etoposide contacts the skin or mucosa, immediately wash the affected area with soap and water.

9. PHYSICAL and CHEMICAL PROPERTIES

VAPOR DENSITY: 1.6 g/m³

SPECIFIC GRAVITY: 1 @ 20°C

SOLUBILITY IN WATER: <1 mg/mL

VAPOR PRESSURE, mm Hg @ 25°C: 45 mm Hg

EVAPORATION RATE (n-BuAc=1): 1.5-2.0

MELTING POINT or RANGE: Not applicable.

BOILING POINT: >200°C.

APPEARANCE and COLOR: Clear, yellow solution

HOW TO DETECT THIS SUBSTANCE (warning properties): This product has no distinct warning properties. The yellow color may be helpful for detection.

10. STABILITY and REACTIVITY

STABILITY: Stable when stored under ambient conditions within the time of the shelf-life of the product. The recommended storage temperature is 25°C.

CONDITIONS TO AVOID: Heat may cause product to decompose, destroying the product or producing toxic fumes.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: Components of the carrier are incompatible with oxidizers.

HAZARDOUS POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Heat and contact with incompatible chemicals.

PART IV *Is there any other useful information about this material?*

11. TOXICOLOGICAL INFORMATION

TOXICITY DATA:

Polysorbate

LD₅₀i_{pr}-rat = 6804 mg/kg

LD₅₀i_{vn}-rat = 1790 mg/kg

LD₅₀oral-mouse = 25 mg/kg

Benzyl alcohol

LD₅₀ oral-rat = 1230 mg/kg

LD₅₀i_{pr}-rat = 400 mg/kg

LD₅₀ oral - mouse = 1580 mg/kg

Etoposide

Mutation data is reported at doses of 1-3% of the clinical dose.
Reproductive effects are reported in mammals at doses below 100 mg/kg.
LD₅₀ oral-rat = 147, 215, and 1784 mg/kg
TDLo oral-human 16 mg/kg
TDLo intravenous-human 2.6 mg/kg
TDLo intravenous-child 183 mg/kg

LD₅₀ intraperitoneal-rat = 39 mg/kg
LD₅₀ subcutaneous-rat >200 mg/kg
LD₅₀ intravenous-rat 75 mg/kg
LD₅₀ oral-mouse = 215 mg/kg
LD₅₀ intraperitoneal-mouse 64 mg/kg
LD₅₀ subcutaneous-mouse - 143 mg/kg
LD₅₀ intravenous-mouse = 15 mg/kg
LD₅₀ intravenous-rabbit = 37 mg/kg

SUSPECTED CANCER AGENT: This material must be considered as a possible human carcinogen. Etoposide and the other components are not found on the following lists: FEDERAL OSHA Z LIST, NTP, IARC, CAL/OSHA. Etoposide is listed as a teratogen by the State of California (Proposition 65).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE:

<u>Dermal Exposure:</u>	Local irritation may occur.
<u>Ingestion Exposure:</u>	Gastrointestinal distress may occur.
<u>Inhalation Exposure:</u>	Any existing respiratory symptoms may be enhanced.

RECOMMENDATIONS TO PHYSICIANS: Refer to adverse reaction information provided with the product.

12. ECOLOGICAL INFORMATION

ENVIRONMENTAL STABILITY: Based on components of this product, the size of the product packaging and shipping, environmental impact is not expected.

EFFECT OF MATERIAL ON PLANTS or ANIMALS: No environmental effect information for this product is currently available. The constituents are sufficiently dilute to expect no impact from a release of the size possible from the packaging and shipping containers.

EFFECT OF CHEMICAL ON AQUATIC LIFE: No direct information is currently available regarding the potential affect of this material on aquatic life.

13. DISPOSAL CONSIDERATIONS

PREPARING WASTES FOR DISPOSAL: Waste disposal must be in accordance with appropriate Federal, State, and local regulations. This product, if unaltered by the handling, may be disposed of by treatment at a permitted facility or as advised by your local hazardous waste regulatory authority.

EPA WASTE NUMBER: Not applicable.

14. TRANSPORTATION INFORMATION

THIS MATERIAL IS HAZARDOUS AS DEFINED BY 49 CFR 172.101 BY THE U.S. DEPARTMENT OF TRANSPORTATION.
U.S. DOT Ground Transportation Requirements

PROPER SHIPPING NAME: Medicines, n.o.s. (contains ethanol)
HAZARD CLASS NUMBER and DESCRIPTION: 3, Flammable liquid
UN IDENTIFICATION NUMBER: NA1993
PACKING GROUP: II
DOT LABEL(S) REQUIRED: Flammable liquid
EMERGENCY RESPONSE GUIDE NUMBER: 27
RQ: none

Shipments of inside containers less than 30 mL and gross mass of less than 29 kg are excepted from most DOT regulations. Refer to 49 CFR 173.4 for specific requirements. In accordance with 49CFR 107.111 the DOT has granted GensiaSicor Pharmaceuticals party status to DOT-E 9275.

15. REGULATORY INFORMATION

FEDERAL LAW prohibits dispensing without a prescription.

SARA REPORTING REQUIREMENTS: The components of this product ARE NOT subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act.

TSCA INVENTORY STATUS: The components of this product are listed on the TSCA Inventory.

MARINE POLLUTANT: This product contains no component listed as a Marine Pollutant under 49 CFR 172.101, Appendix B.

CALIFORNIA PROPOSITION 65: Etoposide is on the California Proposition 65 lists.

CERCLA REPORTABLE QUANTITIES (RQ): Not applicable.

STATE REGULATORY INFORMATION: The following constituent chemicals are subject to special State regulations, as noted below:

Alabama	None	New Hampshire	None
Alaska	Ethyl Alcohol	New Jersey	None
California	Ethyl Alcohol	New York	None
Connecticut	None	North Dakota	Ethyl Alcohol
Delaware	None	Oklahoma	None
Florida	None	Oregon	None
Illinois	None	Pennsylvania	Ethyl Alcohol
Kansas	None	Rhode Island	Ethyl Alcohol
Maine	None	Tennessee	None
Maryland	None	Texas	Ethyl Alcohol
Massachusetts	None	Vermont	None
Michigan	None	Washington	None
Minnesota	None	Wisconsin	Ethyl Alcohol
Missouri	Ethyl Alcohol	West Virginia	None
Montana	None		

LABELING (Precautionary Statements): Etoposide should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Severe myelosuppression with resulting infection or bleeding may occur.

16. OTHER INFORMATION

PREPARED BY: CHEMICAL SAFETY ASSOCIATES, Inc.
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619/565-0302

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