



Material Safety Data Sheet

Toposar[®] Injection

1. PRODUCT IDENTIFICATION

Product Name Toposar[®] Injection
Product Use Medical Treatment; Antineoplastic Agent
Manufacturer Teva Parenteral Medicines, Inc..
Address 11 Hughes
 Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
 1-202-483-7617 (International Collect)
Business Phone 1-800-729-9991
Website Address <http://www.newsicor.com>

Common Names Etoposide Injection, USP
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 6mL, 30mL and 50mLvials

Date of Preparation: December 22, 2005

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	EXPOSURE LIMITS IN AIR					
		Wt%	ACGIH		OSHA		Other
			TLV	STEL	PEL	STEL	
Etoposide	33419-42-0	1.96	NE	NE	NE	NE	0.14-7 ug/m3*
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 C - Ceiling Limit *Several Manufacturers of Etoposide TWA Exposure Limit

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 format

CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.



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3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is clear, yellow solution. Flammable liquid and vapor. Harmful if swallowed or injected. Eye and skin irritant. May cause damage to the bone marrow, reproductive system and liver. Harmful to the fetus. Vapor can cause flash fire. Keep away from heat, sparks, flames, or other sources of ignition (e.g., static electricity, pilot lights, mechanical/electrical equipment). Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Do not taste or swallow. Wash thoroughly after handling.

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness and swelling of the eyes and redness, itching, burning and skin damage. May cause an allergic reaction on the skin.

Ingestion: Ingestion is not an anticipated route of occupational exposure. However, the active ingredient, Toposar®, is toxic if swallowed. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including bone marrow suppression with decreased blood cells, chills, fever, nausea, vomiting, severe gastrointestinal distress, liver disorders, unusual bleeding, severe loss of blood pressure, cardiac irregularities, breathing difficulties and hair loss may occur. See package insert for other adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as fever, nausea, vomiting, and loss of blood pressure may occur.

Cancer: Toposar® has not been specifically tested for cancer (see Section 11 for additional information).

Chronic: Based on animal data, Toposar®, is considered a potential developmental and reproductive toxicant (see Section 11).

Target Organs: Potential hazard to the bone marrow and liver (see Section 11).

Pre-Existing Medical Conditions: Pre-existing skin, bone marrow, reproductive and liver disorders may be aggravated by exposure to this material.



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6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

7. HANDLING and STORAGE

ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from all sources of ignition and any incompatible materials or conditions (see Section 10). Store at 15-30°C (59-86°F).

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile 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.



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8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances where air-purifying respirators may not provide adequate protection. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant a respirator's use.

Eye 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.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	1.6 mg/m ³	Evaporation Rate (n-BuAc=1):	1.5-2.0
Specific Gravity (water = 1):	1 @ 20°C	Melting/Freezing Point:	Not applicable
Solubility in Water:	<1 mg/mL	Boiling Point:	>200°C
Vapor Pressure, mm Hg @ 25°C.	45 mm Hg	pH:	ND
Odor Threshold: ND			
Appearance and Color: Clear yellow solution			

ND = No Data

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: Components of the carrier are incompatible with oxidizers.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Heat may cause product to decompose, destroying the product or producing toxic fumes.



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11. TOXICOLOGICAL INFORMATION

Toxicity Data: The following information is for Etoposide, the active ingredient:

Oral LD50(rat) = 147 mg/kg	IV LD50(rat) = 75 mg/kg	IP LD50(rat) = 39 mg/kg
Oral LD50(rat) = 215 mg/kg	IV LD50(mouse) = 15 mg/kg	IP LD50(mouse) = 64 mg/kg
Oral LD50(Rat) = 1784 mg/kg	IV (LD50)(rabbit) = 37 mg/kg	SubQ(rat) > 200 mg/kg
Oral LD50(mouse) = 215 mg/kg		SubQ(mouse) = 143 mg/kg

Suspected Cancer Agent: The carcinogenic potential of Toposar® (Etoposide) has not been examined in test animals; however, compounds with similar mechanisms of action and mutagenicity profiles have been reported to be carcinogenic. It is not listed as carcinogenic by NTP, IARC or OSHA.

Irritancy of Product: This product is expected to be irritating to contaminated skin, eyes and other tissues.

Sensitization to the Product: Rare instances of allergic reactions have occurred from clinical use of Toposar® (Etoposide and Etoposide Phosphate). No data on allergic sensitization potential from repeated skin contact.

Target Organ(s): Causes bone marrow suppression (decreased white blood cell count and platelets, neutropenia and thrombocytopenia) and changes in the liver.

Reproductive Toxicity Information: Listed below is information concerning the effects of Toposar® (Etoposide) on human and animal reproductive systems. This material is classified as a Pregnancy Category D (Positive evidence of risk). Currently, there have been no studies in pregnant women.

Mutagenicity: Toposar® (Etoposide) is considered mutagenic based on results of in-vitro Ames gene mutation assay and in vivo mouse micronucleus assay.

Embryotoxicity/Teratogenicity/Reproductive Toxicity: Toposar® (Etoposide) causes malformations (birth defects) in the offspring of laboratory animals. Etoposide has been shown to affect the reproductive organs of male and female laboratory animals. In males, effects on testicular size and sperm abnormalities have been reported.

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: It is anticipated that this compound will decompose into a variety of organic compounds.

Effect of Materials on Plants or Animals: This product may be harmful to contaminated plant and animal life. See Section 11 (Toxicological Information) for additional information.

Effect of Chemicals on Aquatic Life: This product may be harmful to aquatic plant and animal life in contaminated bodies of water, especially if released in large quantities.



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13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: D001

14. TRANSPORTATION INFORMATION

This Material is Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation. The following is a list of options for shipping this drug:

Proper Shipping Name: Ethanol solutions,

Hazard Class Number and Description: 3

UN Identification Number: UN1170

Packing Group: II

DOT Label(s) Required: Flammable liquid

North American Emergency Response Guidebook Number (1996): 128

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Proper Shipping Name: Consumer commodity ORM-D

Hazard Class Number and Description: None

UN Identification Number: None

Packaging Group: None

DOT label(s) Required: None

DOT Exemption SP 9275 – Teva Parenteral Medicines, Inc. is party to this exemption which permits shipment of certain limited quantities of ethanol containing materials. The exemption authorizes a person who is not a holder of this exemption to reoffer it for transportation provided no modifications or changes are made to the package and it is reoffered for transportation in conformance with this exemption and the Hazardous Materials Regulations. A copy of Teva Parenteral Medicines, Inc. exemption must be maintained at each facility where this drug is offered or reoffered for transportation.

Transport Canada Transportation of Dangerous Goods Regulations: This material is considered as dangerous goods. See above.



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15. REGULATORY INFORMATION

U.S. REGULATIONS

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. TSCA Inventory Status: Toposar[®] is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product contains chemicals (Ethanol, Etoposide) known to the State of California to cause cancer or reproductive effects.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne Pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS

Canadian DSL/NDSL Status: Toposar[®] is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): DANGER! Flammable Liquid. Accidental Ingestion or Injection May Be Harmful. Eye and skin irritant. Harmful to the Fetus. May Cause Damage to the Bone Marrow, Liver and Reproductive System. Toposar[®] should be administered under the supervision of a qualified physician. Vapor can cause flash fire. Keep away from heat, sparks, flames, or other sources of ignition (e.g., static electricity, pilot lights, mechanical/electrical equipment). Avoid over-exposure. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy. Avoid accidental injection. Do not eat, drink or smoke when handling. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

16. OTHER INFORMATION

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