Getwell Pharmaceuticals
474, Udyog Vihar, Phase-V,
Gurgaon - 122 016, Haryana, INDIA

Etoposide Injection

Section I - IDENTITY

Common/Trade Name: Etoposide Injection (20mg/ml, available in 5ml vials)

Chemical Names: 9-((4,6-0-Ethylidene-beta-D-glucopyranosyl)oxy)-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)furo(3',4':6,7)naphtho(2,3-d)-1,3 dioxol-6-(5ah)-one

Synonyms: Etopa

Manufacturer's Name: GETWELL PHARMACEUTICALS
Address: 474, UDYOG VIHAR, PHASE-V,
GURGAON - 122 016, HARYANA, INDIA

Telephone Number for Info.: +91 124 4014 403 / 04

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Section II - HAZARDOUS INGREDIENTS/COMPOSITION INFORMATION

This product is an ethanol solution containing the following compounds.

Component	%	CAS#	OSHA PEL	ACGIH TLV	Other Limits Recommended
Etoposide	2	33419-42-0	NONE	NONE	0.7 - 3.5 mcg/m3
Polyethylene Glycol 300	57	25322-68-3	NONE	NONE	NONE
Ethyl Alcohol	30	64-17-5	1000ppm	1000ppm	NONE
Polysorbate 80	7	9005-65-6	NONE	NONE	NONE
Benzyl Alcohol	3	100-51-6	NONE	NONE	NONE
Citric Acid	1	77-92-9	NONE	NONE	NONE

Etoposide is a sterile injectable liquid drug provided in a vial.

Section III - HEALTH HAZARD DATA

Routes of Entry: This material may be harmful if swallowed or injected into the skin. Exposure may also occur via inhalation.

Health Hazard (Acute & Chronic): Etoposide is a cytotoxic anticancer drug used for the treatment of testicular and small cell lung cancers. Exposure to Etoposide may cause adverse effects to the digestive system, irritation, or allergic reaction and may affect the blood forming system and respiratory system. Various gastrointestinal and allergic reactions have been reported.

Carcinogenicity: **NTP?** NO **IARC Monographs?** Group 2A- Probable Carcinogen Limited Evidence

OSHA Regulated? NO

Etoposide is considered a potential carcinogen due to mode of action and is known to cause birth defects.

Signs & Symptoms of Exposure: Contact with the skin may cause irritation or local allergic reaction. Nausea and vomiting may occur after ingestion of therapeutic doses; acute ingestion may result in severe gastrointestinal distress. Ingestion of this product may lead to bone marrow suppression and associated loss of blood cells, GI problems, sudden severe loss of blood pressure, allergic reactions characterized by fever, chills, cardiac irregularities, and breathing difficulties. Other symptoms may include hair loss, after-taste and vision difficulty.

Medical Conditions Generally Aggravated by Exposure: Exposure could aggravate GI tract disorders and respiratory system disorders.

BVL Hazard Category: 4

Section IV - FIRST AID MEASURES

Eye Exposure: Flush eyes with large volumes of water for 15 minutes.

Skin Exposure: Wash skin with cool, soapy water.

Ingestion: If ingestion occurs, flush mouth out with water and seek medical attention immediately. If person in conscious, induce vomiting. Never induce vomiting on an unconscious person.

Inhalation: If difficulty breathing, administer oxygen. Seek attention of a physician immediately. If necessary, provide artificial respiration.

There is not antidote for overdose. Treat person symptomatically.

Section V - FIRE AND EXPLOSION HAZARD DATA

Flash Point (Method Used): 21°C (70°F)

Flammable Limits: LEL: 3.3% **UEL:** 24.5%

Extinguishing Media: Use water or an ABC multi-purpose fire extinguisher.

Special Fire Fighting Procedures: As with all fires, evacuate personnel to a safe area. Fire fighters should wear a self-contained breathing apparatus to avoid inhalation of smoke.

Unusual Fire/Explosion Hazards: Ethyl alcohol is flammable. Keep this product away from ignition sources.

Section VI - ACCIDENTAL RELEASE INFORMATION

Release to Land: Since Etoposide is a flammable solution, remove all sources of ignition. Absorb Etoposide with activated charcoal or absorbent pads and dispose of according to local, state, and federal guidelines. Wash area of spill with a bleach solution followed by soap and water to remove product.

Release to Air: If aerosolized, reduce exposures by ventilating area; clean up spill immediately to prevent evaporation.

Release to Water: Refer to local water authority. Drain disposal must not occur.

Section VII - PRECAUTIONS FOR SAFE HANDLING AND USE

Steps to be taken in case material is released or spilled: See Section VI above; wear latex or nitrile gloves and safety glasses. If vapors are generated, an appropriate respirator with organic vapor cartridges must be worn. For larger spills, additional protective clothing and respirator protection may be needed such as chemical protective coveralls, boots, double gloves (neoprene), and self contained breathing apparatus (SCBA).

Waste Disposal Method: Incineration in an approved incinerator for flammable liquids according to local, state, and federal guidelines.

Precautions to be taken in handling and storing: Store at room temperature (15-30°C).

Other Precautions: Follow OSHA guidelines on the safe handling of anti-cancer drugs (see Section XVI).

Section VIII - CONTROL MEASURES AND PERSONAL PROTECTIVE EQUIPMENT

Respiratory Protection: Under normal use, respirators are not required. If aerosols/vapors are generated, an air-purifying respirator with organic vapor cartridges for large spill emergencies SCBA may be required. Personnel wearing respirators should be fit tested and approved for respirator use under the OSHA Respiratory Protection Standard 29 CFR 1910.134.

Ventilation: Handle in a Type II Biological Safety Hood or in a well-ventilated area.

Protective Gloves: Latex or nitrile

Eye Protection: Safety glasses or splash goggles

Other Protective Clothing or Equipment: Lab coat

Work/Hygienic Practices: Wash hands following use. No eating, drinking, or smoking while handling this product.

Section IX - PHYSICAL/CHEMICAL CHARACTERISTICS

Physical State: Liquid

Appearance and Odor: Clear, yellow negligible odor

Boiling Point: 78°C

Vapor Pressure mm Kg @ 25°C: 45 mm Hg

Vapor Density: approx. 1

Specific Gravity: approx. 1

Melting Point: not applicable

Evaporation Rate: not available

Solubility in Water: <1 mg/ml

pH: 3-4

Section X - STABILITY AND REACTIVITY DATA

Stability: Stable at room temperature
Incompatibility (Materials to Avoid): This product is not compatible with strong bases and oxidizers.
Hazardous Decomposition or Byproducts: Decomposition products of this compound may include potentially hazardous byproducts of nitrogen oxides, carbon monoxide, and carbon dioxide.
Hazardous Polymerization: Will not occur
Conditions to Avoid: Storage next to strong oxidizers.

Section XI - TOXICOLOGICAL INFORMATION

Etoposide: RTECS # KC0190000

LD_{50} oral, rat = 1784 mg/kg
LD_{50} intraperitoneal, rat = 39 mg/kg
LD_{50} subcutaneous, rat = >200 mg/kg
LD_{50} intravenous, rat = 58 mg/kg
LD_{50} oral, mouse = 215 mg/kg
LD_{50} intraperitoneal, mouse = 64 mg/kg
LD_{50} intravenous, mouse = 15070 ug/kg

Data for Polysorbate 80: RTECS # WG2932500

LD_{50} intraperitoneal, rat = 6804 mg/kg
LD_{50} oral, mouse = 25 mg/kg
LD_{50} intravenous, rat = 1790 mg/kg

Data for Benzyl Alcohol: RTECS # DN3150000

LD_{50} oral, rat = 1230 mg/kg
LD_{50} intraperitoneal, rat = 400 mg/kg
LD_{50} oral, mouse = 1360 mg/kg

Toxicity for final solution is derived from active drug substance.
Toxicity data is not available for the final product.
Additional reproductive health data is available from the National Institute for Occupational Safety and Health (NIOSH) Registry of Toxic Eff ects of Chemical Substances (RTECS).

Section XII - ENVIRONMENTAL IMPACT INFORMATION

Information is currently not available on the environmental impact of Etoposide. Handle in a manner to prevent spills or releases to the environment.

Section XIII - DISPOSAL INFORMATION

Dispose of by hazardous waste incineration at an approved/permitted facility according to local, state, and federal guidelines. Etoposide is a flammable waste EPA code: D001

Section XIV - TRANSPORTATION INFORMATION

Etoposide is a Hazardous Material per 49 CFR 172.101
Proper Shipping Name: Ethanol Solutions
Hazard class: 3 (Flammable liquid)
UN ID Number: UN 1170
Label and Placards: Flammable Liquid
Packing Group: II
Emergency Response Guide: 131
The chemicals in this product are not classified as DOT Marine Pollutants

Section XV - REGULATORY INFORMATION

SARA 313 listed?: NO
CERCLA listed?: NO
RCRA listed?: YES -- Etoposide is a characteristic flammable waste D001
Listed on California's Proposition 65 list: Code D

Section XVI - OTHER DATA

1. Use of this product should be through or under the direction of a physician. This MSDS does not address the therapeutic use of this material.

2. Hospital personnel preparing or administering parenteral antineoplastic agents should wear disposable latex gloves, safety glasses, a closed-front gown with cuffs and respiratory protection. Preparation of all antineoplastic agents should be done in a class II laminar flow hood or biological safety cabinet with exhaust air discharged external to the room environment. All needles, syringes, vials, and other equipment or disposable clothing that have contacted this agent should be segregated for incineration.

3. Persons administering this drug to patients must be careful to avoid needle sticks to syringes and other sharps used in the administration. All needle sticks must be reported to your company management.

4. BVL Hazard Category Definitions (internal hazard ranking used by Ben Venue Laboratories): 1 = Low Toxicity
   2 = Moderate Toxicity
   3 = Potent or Toxic
   4 = Highly Potent or Toxic
   5 = Extremely Potent or Toxic

5. OEL=Occupational Exposure Limit. An internal limit set by Getwell Pharmaceuticals for the recommended limit of employee exposure to airborne dusts or aerosols that should not be exceeded over an eight-hour time-weighted average.

6. Etoposide is considered a Hazardous Drug as described in the NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings . Employees who prepare or administer hazardous drugs or who work in areas where these drugs are used should follow specific handling guidelines in order to prevent exposure to these agents in the air or on work surfaces, clothing, or equipment.

7. **The Following Guidance Information is excerpted from the NIOSH Alert:**

Elements of a Hazardous Drug Handling Program include:

- Establishment and implementation of written policies and protocols to ensure the safe handling of oncolytic and/or potent drugs, including receipt of product.
- Training and education of employees on the recognition, evaluation and control of Hazardous Drugs
- Effective Planning and design of the workplace
- Use of best practice control measures and specialized equipment such as ventilated cabinets or isolators designed for worker protection
- Wearing recommended personal protective equipment
- An integrated health surveillance program that: includes the assessment and counseling of prospective employees before they commence any work involving oncolytic and/or potent drugs and related waste

8. **Published guidance on the handling and transport of cytotoxic drugs:**

NIOSH Alert – Preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings

http://www.cdc.gov/niosh/docs/2004-165/

National Study Commission on Cytotoxic Exposure: Recommendation for handling Cytotoxic Agents:

http://www.nih.gov/od/ors/ds/pubs/cyto/index.htm