Fresenius Kabi Oncology Limited
Echelon Institutional Area, Plot No. - 11
Sector - 32, Gurgaon, Haryana, India

FRESENIUS KABI

SAFETY DATA SHEET
ETOPOSIDE INJECTION

1. SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1. Product Identifier	Etoposide Injection
Synonyms	4-demethylepipodophyllotoxin 9-[4,6-0-(R)-ethylidine-b-D-glucopyranoside
1.2. Relevant identified uses of the substance or mixture and uses advised against intended use	Antineoplastic
1.3. Details of the supplier of the safety data sheet	Fresenius Kabi Oncology Ltd Echelon Institutional Area, Plot No-11 Sector-32, Gurgaon-122001, Haryana, India Telephone number: +911244885000 Contact E-Mail: nagesh.shrivastava@fresenius-kabi.com
1.4. Emergency Telephone number	+911244885463

2. SECTION 2: HAZARDS IDENTIFICATION

2.1.Classification of substance or mixture

EU Classification

According to Article 1, item 5(a) of CLP Regulation (EC) 1272/2008, medicinal products in finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

GHS Classification	Flammable Liquids	Category 2
	Mutagenic	Category 2
	Toxic to Reproduction	Category 2
	Carcinogenic	Category 1B

2.2. Label Elements

Signal Word Warning

Pictogram

Hazards Statements

H225 - Highly flammable liquid and vapor
H350 - May cause cancer
H340- May cause genetic defects,
H360-May damage fertility or the unborn child
H319-Causes serious eye irritation

Precautionary Statements

P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P210 - Keep away from heat/sparks/open flames/hot surfaces. - No smoking
P233 - Keep container tightly closed
P260 - Do not breathe fumes/vapours/spray.
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P403 + P235 - Store in a well-ventilated place. Keep cool
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations
P370 + P378 - In case of fire: Use CO_2, extinguishing powder, foam, or water for extinction

P305 + P351 + P338+P337+P313- IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.

2.3. Other hazards No data available for PBT and vPvB or any other hazard

3. SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Not applicable

3.2 Mixtures

Ingredients	Quantity in mg / ml	CAS No	EC No	Index No	Registration No	Classification according to Regulation (EC) No 1272/2008
Etoposide	20.0 mg	33419-42-0	251-509-1	-	-	AcuteTox.4; Carc.1B; H302,H350
Ethanol anhydrous	EXCIPIENTS	64-17-5	200-578-6	603-002-00-5	-	Flam.Liq.2;Eye irrit.2;H225,H319
Anhydrous Citric acid		77-92-9	201-069-1	-	-	Eye irrit.2; H319
Benzyl alcohol		100-51-6	202-859-9	603-057-00 5	01-2119492630 -38-XXXX	AcuteTox.4;Eye irrit.2;H302+H332, H319
Polysorbate 80		9005-65-6	-	-	-	Not a hazardous substance or mixture
Macrogol 300		25322-68-3	-	-	-	Not classified according to the CLP regulation.

4. SECTION-4 FIRST AID MEASURES

4.1 Description of first aid measures

Eye Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur seek medical attention. Provide Symptomatic / supportive care as necessary.
Skin Contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/ supportive care as necessary.
Inhalation	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic /supportive care as necessary.
Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

4.2 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 2 – Hazards Identification and/or Section 11 - Toxicological Information.
Medical Conditions Aggravated by Exposure: None known

4.3. Indication of any immediate medical attention and special treatment needed

Victims of exposure must be taken for medical attention. Take a copy of the SDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians' Desk Reference for additional treatment information.

5. SECTION 5: FIRE FIGHTING MEASURES

5.1. Extinguishing media

Carbon dioxide, dry chemical extinguishing powder or foam.
Not recommended extinguishing media: no data available.

5.2. Special hazards arising from the substance or mixture

When heated, product may produce combustible vapors due to the alcohol content. Keep away from flames, sparks, and other sources of ignition.

5.3. Advise for fire fighters

No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self-contained breathing apparatus.

6. SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures

6.1.1. For non-emergency personnel

Avoid contamination with the product.

Notify the effected individuals of the emergency, to be aware of the issues associated.

Avoid contact of the product with skin and eyes.

Remove contaminated clothing and wash before reuse.

6.1.2. For emergency responders

Wear personal protective equipment. Ensure adequate ventilation. Never return spills in original containers for re-use.

6.2. Environmental precautions

Do not flush into surface water or sanitary sewer system.

6.3. Methods and material for containment and cleaning up

Isolate the area around spill and remove all sources of ignition. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable inert material and clean affected area with soap and water. Absorb the liquid with an inert absorbent material (e.g. absorbent pad). Clean again with soap and water. Dispose of spill materials according to applicable national, state, or local regulations.

6.4. Reference to other sections

Use the control measures and personal protective equipment described in section 8 of this SDS. Refer to section 13 of this SDS for disposal considerations.

7. SECTION 7: HANDLING AND STORAGE

7.1. Precautions for safe handling

Etoposide is anti-neoplastic agent. Appropriate procedures should be implemented during the handling and disposal of anti-neoplastics agents to minimize potential exposures. Several guidelines on handling anti-neoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

Avoid ingestion, inhalation, skin contact, and eye contact. If handling the powder, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilization of this antineoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials may be required when working with this material.

7.2. Conditions for safe storage, including any incompatibilities

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for anti-neoplastic agents. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert. Store at controlled room temperature 15 ^{o}C to 30^{o} C. Keep away from food, and drink. Advice on Segregation

7.3. Specific end use(s)

No data available.

8. SECTION 8: EXPOSURE CONTROL/PERSONAL PROTECTION

8.1. Control parameters

Components with workplace control parameters

	Exposure limits		
Component	**OSHA-PEL**	**ACGIH-TLV**	**AIHA WEEL**
Etoposide	8-hrTWA:Not established	8-hrTWA:Not established	8-hrTWA:Not established

Etoposide-OEL TWA-8Hr: 0.7 µg/m3

Notes

OSHA-PEL; US Occupational Safety and Health Administration-Permissible Exposure Limit

ACGIH-TLV; American Conference of Governmental Industrial Hygienists-Threshold Limit Value

AIHA WEEL; Work Place Environmental Exposure Level

TWA; 8 hour Time weighted Average

Occupational Exposure Limit- Reference Material Safety data sheet of Pfizer, Inc.

8.2Exposure control

8.2.1. Appropriate engineering controls

Local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

8.2.2. Individual protection measures, such as personal protective equipment

Protective clothing should be selected specifically for the working place, depending on concentration and quantity of the hazardous substances handled.

a) Eye / Face 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.

b) Skin protection: When handling this product, disposable gloves should be worn at all times. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to chemotherapy agents. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

c) Respiratory protection: Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

d) Thermal hazards:

Not applicable

8.2.3. Environmental exposure controls

No data available.

9. SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Appearance/Physical state	Liquid Solution
Odor	NA
Odor threshold	NA
PH	NA

Melting point/Freezing point	NA
Initial Boiling point /Boiling Point Range	NA
Flash point	13° C(Method-Closed cup)
Evaporation rate	NA
Flammability (solid, gas)	NA
Upper/lower flammability or Explosive limits	NA
Vapor pressure	45 mm Hg at 25° C
Vapor density (Air=1)	NA
Relative density	NA
Solubility	Etoposide is sparingly soluble in water and ether. Very soluble in methanol, and chloroform.
Partition coefficient (n-octanol/water)	NA
Auto-ignition temperature	NA
Decomposition temperature	NA
Viscosity	NA

10. SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Not determined.

10.2. Chemical stability

Stable under normal temperature and pressures.

10.3. Possibilities of hazardous reactions

Not determined.

10.4. Conditions to avoid

Heat, flames, sparks or other sources of ignition.

10.5. Incompatible materials

Not determined.

10.6. Hazardous decomposition products

Not determined. Thermal decomposition products may include smoke and toxic fumes. Oxides of carbon and Oxides of nitrogen may formed.

11. SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects- The information included in this section describes the potential hazards of the individual ingredients.

a) Acute Toxicity:

Etoposide

Species	Route	End Point	Dose
Rat	Oral	LD 50	1784 mg/kg
Rat	Para-periosteal	LD 50	58 mg/kg
Mouse	Oral	LD 50	215 mg/kg
Mouse	Intravenous	LD 50	15.07 mg/kg
Rabbit	Oral	LD 50	147 mg/kg

Ethanol

Species	Route	End Point	Dose
Mouse	Oral	LD 50	3450 g/m3
Rat	Oral	LD 50	7060 mg/kg
Mouse	Inhalation	LC 50 4h	39 g/m3
Rat	Inhalation	LC 50 10 h	20000 ppm

Citric acid

Species	Route	End Point	Dose
Rat	Oral	LD 50	3000 mg/kg

b) Irritation / Sensitization:

Ethanol

Study Type	Species	Severity
Eye irritation	Rabbit	Severe

Macrogol 300

Study Type	Species	Severity
Eye irritation	Rabbit	Mild
Skin irritation	Rabbit	Mild

Citric acid

Study Type	Species	Severity
Eye irritation	Rabbit	Severe
Skin irritation	Rabbit	Mild

c)Repeated Dose Toxicity:

Etoposide

Duration	Species	Route	Dose	End Point	Target Organ
3Month(s)	Rat	Intravenous	0.5 mg/kg/day	LOAEL	Male reproductive system
1Month(s)	Rat	Intravenous	0.15 mg/kg/day	LOAEL	Blood forming organs, Bone Marrow, Gastrointestinal system, Male reproductive system, Peripheral nervous system

d) Reproduction & Developmental Toxicity:

Etoposide

Study Type	Species	Route	Dose	End Point	Effect(s)
Embryo/ Fetal Development	Mouse	Intraperitoneal	0.5 mg/kg/day	LOAEL	Teratogenic
Embryo/ Fetal Development	Rat	Intravenous	0.13 mg/kg/day	LOAEL	Developmental toxicity

Embryo/ Fetal Development	Mouse	Intravenous	1.2 mg/kg/day	LOAEL	Fetotoxicity, Teratogenic
Embryo/ Fetal Development	Mouse	Intraperitoneal	1.5 mg/kg/day	LOAEL	Fetotoxicity, Teratogenic
Embryo/ Fetal Development	Mouse	Intraperitoneal	2.0 mg/kg	LOAEL	Fetotoxicity, Teratogenic

e) Genetic Toxicity:

Etoposide

Study Type	Cell Type/Organism	Result
In Vitro Chromosome Aberration	Mouse	Positive
In Vitro Sister Chromatid Exchange	Chinese Hamster Ovary (CHO) cells	Positive
In Vitro Mammalian Cell Mutagenicity	Chinese Hamster Ovary (CHO) cells	Positive
In Vivo Micronucleus	Rat Bone Marrow	Positive
In Vitro Chromosome Aberration	Human Lymphocytes	Positive

f)Carcinogen Status:

Etoposide

IARC	Group 1 (Carcinogenic to Humans)
OSHA	Listed

Ethanol

IARC	Group 1 (Carcinogenic to Humans)
OSHA	Listed

h) STOT - single exposure: NA

j) Aspiration toxicity: None anticipated from normal handling of this product.

Toxicological information- Reference Material Safety data sheet of Pfizer, Inc

12. SECTION 12 ECOLOGICAL INFORMATION

12.1.Toxicity

Not determined for product. Information for Etoposide is as follows:

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)
Etoposide
Oncorhynchus mykiss (Rainbow Trout) LC50 96 Hours 12,900 mg/L
Pimephales promelas (Fathead Minnow) LC50 96 Hours 14,200 mg/L
Daphnia Magna (Water Flea) EC50 48 Hours > 61.8 mg/L

Aquatic Toxicity- Reference Material Safety data sheet of Pfizer, Inc

12.2. Persistence and degradability

Not determined for product.
Ethanol was reported to be degraded between 45% and 74% in five days in two aqueous biodegradation assays.

12.3. Bioaccumulative potential

Not determined for product. Ethanol is not anticipated to bioaccumulate.

12.4. Mobility in soil

Not determined for product

12.5. Result of PBT and vPvB assessment

No data available

12.6. Other adverse effects

No data available

13. SECTION 13 DISPOSAL CONSIDERATIONS

13.1 Waste treatment method

Waste Disposal	All waste materials must be properly characterized. Further, disposal should be performed in accordance with the national, state or local regulatory requirements.
Container Handling and Disposal	Dispose of containers and unused contents in accordance with national, state and local regulations.

14. SECTION 14 TRANSPORT INFORMATION

14.1 UN number

UN 1170

14.2 UN proper shipping name

Ethanol Solution

14.3 Transport hazard class(es)

3

14.4 Packing group

II

14.5 Environmental hazards

NA

14.6 Special precaution for user

NA

14.7 Transport in bulk according to Annex II of Marpol and the IBC code

NA

15. SECTION 15: REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or Mixture

US TSCA Status	Not listed. However, ethyl alcohol, benzyl alcohol, citric acid, Macrogol300 and Polysorbate80 is listed on the TSCA inventory.
US CERCLA Status	Not listed

US SARA 302 Status	Not listed
US SARA 313 Status	Not listed
US RCRA Status	Not listed
US PROP 65 (Calif.)	Listed development. Ethyl alcohol in alcoholic beverages is known to the State of California to cause cancer and developmental toxicity.
Notes: TSCA, Toxic Substance Control Act; CERCLA. US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65	

15.2 Chemical safety assessment

No Chemical safety assessment has been carried out for the product.

16. OTHER INFORMATION

Sources of data	Information from published literature and Material Safety Data Sheet of the product Etoposide Solution for Injection published by Pfizer Inc. 235 East 42nd Street, New York, New York 10017
Abbreviations	**ACGIH TLV** - American Conference of Governmental Industrial Hygienists-Threshold Limit Value, **CAS**- Chemical Abstracts Services Number; **CERCLA**- US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act, **LD5o**- Dosage producing 50% mortality, **NA**- Not applicable/Not available, **NE**- Not established, **OSHA PEL** - US Occupational Safety and Health Administration-Permissible Exposure Limit; **Prop 65**- California Proposition 65, **RCRA**- US EPA, Resource

	Conservation and Recovery Act, **SARA** - Superfund Amendments and Reauthorization Act; **STEL** -15-minute Short Term Exposure Limit; **STOT- SE**-Specific Target Organ Toxicity - Single Exposure, **TSCA** - Toxic Substances Control Act; **TWA** – 8-hour Time Weighted Average; **OEL**-Occupational Exposure Limit; **IARC**-International Agency for Research on Cancer;**LC50**-Lethal Concentration 50
Disclaimer	The information and recommendations contained herein are based upon tests believed to be reliable. However, Fresenius Kabi Oncology Limited does not guarantee their accuracy or completeness NOR SHALL ANY OF THIS INFORMATION CONSTITUTE A WARRANTY, WHETHER EXPRESSED OR IMPLIED, AS TO THE SAFETY OF THE GOODS, THE MERCHANTABILITY OF THE GOODS, OR THE FITNESS OF THE GOODS FOR A PARTICULAR PURPOSE. Adjustment to conform to actual conditions of usage may be required. Fresenius Kabi Oncology Limited assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied.