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Prepared by: Greg Baker

#### **Section 1 Chemical Product and Company Identification**

Product Name	Eribulin Mesylate Injection
<b>Drug Substance Name</b>	Eribulin Mesylate
Synonyms	E7389, BOLD, NSC-707389
<b>Eisai Material Numbers</b>	190232
Manufacturer/Supplier	Eisai Inc.
	Woodcliff Lake, NJ 07677
<b>Telephone Number</b>	877-873-4724
24 Hour Emergency Number	CHEMTREC 800-424-9300
	Internationally 703-527-3887
Fax Number	201-746-3207

#### **Section 2 Hazards Identification**

Eribulin is a synthetic derivative of halichondrin B, a potent microtubule inhibitor isolated from marine sponges. Eribulin blocks mitosis by binding to the ends of microtubules, forming abnormal, shortened mitotic spindles that do not pass the spindle checkpoint when dividing cells attempt to transition from metaphase to anaphase. It also reduces the degree of dynamic interaction between microtubules and centromeres during cell division, and inhibits tubulin polymerization. Eribulin is for the treatment of a variety of solid tumors.

Effects seen in clinical trials as a monotherapy were neutropenia/febrile neutropenia, fatigue, and neuropathy. When given to patients with refractory to other chemotherapies, adverse effects included asthenia/fatigue, neutropenia, alopecia, nausea, vomiting, anorexia, fever, leucopenia, anemia, diarrhea, and neuropathy. Mechanism of action suggests a potential to cause adverse effects on fertility; in addition, mechanism as well as positive genotoxicity suggest a potential for oncogenicity.

Occupational Exposure Limit (OEL) for the active ingredient:  $0.1 \mu g/m^3$  Acceptable Surface Limit (ASL) for the active ingredient:  $0.05 \mu g/cm^2$ 

#### **Potential Health Effects:**

Routes of Entry	Ingestion, Inhalation, Skin contact/absorption, Injection, Eye Contact
Inhalation	No information regarding inhalation



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Eye Contact	No information regarding eye irritation
Skin Contact	No information regarding skin irritation
Ingestion	No information regarding ingestion

# **Section 3** Composition/ Information on Ingredients

<b>Chemical Composition</b>	% Composition	<b>Exposure Limits</b>
Eribulin Mesylate	0.05%	$0.1  \mu g/m^3$
Dehydrated Alcohol	4%	1000 ppm
Water for Injection	95.8%	

CAS #	44105-17-6 (Eribulin Mesylate)
NIOSH/RTECS NO.	Not established
Molecular Formula	$C_{22}H_{22}N_2O_6$
Molecular Weight	826.0

### **Section 4** First Aid Measures

The following general precautions should be observed.

Ingestion	Consult a physician immediately. Never give anything by
	mouth to someone who is unconscious or convulsing.
Inhalation	Move victim to fresh air and keep them warm and quiet. If not
	breathing, administer artificial respiration. Get immediate
	medical attention.
Injection	For accidental injection, consult a physician immediately
Eye contact	Flush eyes with clean running water for at least 15 minutes.
	Contact a physician.
Skin	Flush skin with water for at least 15 minutes. Remove and
contact	discard contaminated clothing and shoes. Contact a physician

# **Section 5** Fire Fighting Measures

Flash Point (Closed Cup)	Not established (NE)	
Flammable Limits	Upper - NE % Lower - NE %	
Autoignition Temperature	Not established	
Extinguishing Media	Non-flammable. Use dry chemical, carbon	



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	dioxide, foam or water spray as appropriate for
	the surrounding fire and materials.
Special Fire Fighting	Wear protective clothing and self-contained
Procedures	breathing apparatus as appropriate for
	surrounding fire. Firefighters Should Wear
	Proper Protective Equipment And Self-
	Contained Breathing Apparatus With Full
	Facepiece Operated In Positive Pressure Mode.

#### Section 6 Accidental Release Measures

Prevent migration into the environment. Absorb material and place waste into appropriate container, being careful to prevent contact with broken glass (e.g., utilize a tool to pick up broken glass). Wipe the spill area several times (3 times minimum) with 100% Ethanol. Appropriately discard all clean up materials per local, state, and federal regulations.

For significant liquid spills or spills in a dried state, appropriately trained personnel must use Level B protective safety gear as well as a Powered Air Purifying Respirator (PAPR) or a Self Contained Breathing Apparatus (SCBA) with full facepiece operated in positive pressure mode. Clean up spills in a manner that does not aerosolize the spilled material. Utilize the same methods as described above for absorbing spills, utilizing 100% Ethanol, and discarding of waste.

## **Section 7 Handling and Storage**

Handling	Observe all precautions contained on product label and package
Practices	insert. Aerosol generating activities must be done within an
	appropriate engineering control. Wet wipe any potentially
	contaminated surfaces with a suitable solvent. See Section 8 for
	additional Exposure Controls and Personal Protection guidance.
Storage	This drug should be stored at ≤ 25 degrees C.
Practices	

# **Section 8 Exposure Controls/Personal Protection**

<b>Ventilation</b> If the procedures have a potential for aerosolization, they
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	should be handled in an appropriate engineering control (e.g., Containment System and/or Local Exhaust Ventilation).
Respiratory Protection	None required when aerosolization potential does not exist or if there are adequate engineering controls. Use an appropriate respirator to compliment the effectiveness of engineering controls as needed.
Eye/Skin Protection	As appropriate, wear chemically resistant gloves, safety glasses, and lab coats or body covering to minimize potential for skin contact. If there is the potential for splashes to the face/eyes, safety goggles and/or face shield may be needed in place of safety glasses.

# **Section 9 Physical and Chemical Properties**

<b>Boiling Point</b>	Not Established
Vapor Pressure(Mm Hg)	Not Established
Melting Point	N/A
Density	0.99 g/ml at 25 degrees C
<b>Evaporation Rate</b>	Not Established
Hygroscopicity	Hygroscopic
Ph (Aqueous)	6.0 - 9.0
Solubility	Ethyl Alcohol readily at room
	temperature. Water: 10.4 mg/ml
% Volatiles By Volume	Not Established
Appearance & Odor	Clear colorless solution

# **Section 10 Stability and Reactivity Data**

Stability	Decomposes in acidic conditions
<b>Hazardous Polymerization</b>	Unknown
Conditions To Avoid	Hygroscopic. Moisture, Acidity,
	Temperatures above 25 degrees C
<b>Decomposition Products</b>	Unknown
Incompatible materials	Unknown



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# **Section 11 Toxicological Information**

Mechanism of Action:	Antimitotic agent working via inhibition of tubulin polymerization.
Toxicity:	LD <sub>10</sub> (IV-Mouse)- Not Determined Single doses of 0.75 mg/kg were lethal to rats and two doses of 0.075 mg/kg were lethal to dogs. The no-observed-adverse-effect level (NOAEL) in rats and dogs were 0.015 and 0.0045 mg/kg/day respectively.
Carcinogenicity:	NTP: N/D IARC: N/D Z List: N/D OSHA Reg: N/D
Teratogenicity	Positive in mouse lymphoma mutagenesis assay. Probable carcinogen and teratogen, based on mechanism of action (Antimitotic).
<b>Effects Of Overexposure</b>	Unknown
Target Organs	Testes, intestine, bone marrow, and lymphoid tissue
Medical Conditions	None identified
Generally Aggravated By Exposure	
Routes Of Entry	Inhalation, Ingestion, Eye/Skin Contact, Injection

# **Section 12 Ecological Information**

Study	Result
Acute <i>Daphnia</i>	EC50: 0.79 mg/L
Activated Sludge Respiratory Inhibition	EC50: > 100 mg/L
Ready biodegradability	Not readily biodegradable
Octanol-water partition coefficient	Log Kow = 2.25

Eribulin Mesylate should be considered very toxic to aquatic organisms and is not readily biodegradable. Eisai has established an Acceptable Discharge Limit (ADL) of  $0.9~\mu g/L$ . This value should be adequately protective for the potential environmental effects, and is also protective of human health. Local regulations should be evaluated, as well as regulatory authorities consulted, to determine if this concentration may be used as a facility discharge rate or would be required



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at each drain or whether a facility's dilution waters may be used to achieve this concentration. If this ADL can not be achieved, the facility should send the collected water discharge to an appropriately permitted incinerator for disposal.

### **Section 13 Disposal Considerations**

Disposal Procedure: Dispose in accordance with all applicable federal, state, and local environmental regulations.

### **Section 14 Transportation Data and Additional Information**

Not a hazardous material for transport, and therefore not subject to any domestic, international, or modal transportation regulations.

### **Section 15 Regulatory Information**

Non-regulated

#### **Section 16 Other Information**

In case of overexposure, please contact CHEMTREC 800-424-9300, Internationally 703-527-3887

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