

SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

General



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Product identifier

Istodax[®] (Romidepsin for Injection), Diluent Solution (Vial #2 of 2)

Synonyms

Romidepsin for Injection, Diluent Solution for Istodax

Trade names

Diluent for Istodax[®]

Chemical family

Mixture

Relevant identified uses of the substance or mixture and uses advised against

Bulk solution packaged in vial and supplied in a dual-pack configuration; for use in reconstitution for the final user. Drug product is indicated for the treatment of certain types of cancer.

Note

The toxicological and ecological properties of this product/mixture and/or its ingredients have not been fully characterized. This SDS will be revisited as more data become available. There is a parallel diluent vial in the packaged product (Vial #1). Consult parallel SDS for Istodax[®] for Injection Vial #1 for additional hazard information.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

**Globally Harmonized
System [GHS]** Flammable liquid - Category 4.

SECTION 2 - HAZARDS IDENTIFICATION ...continued

Label elements

| | |
|-------------------------------------|---|
| GHS hazard pictogram | None required |
| GHS signal word | Warning |
| GHS hazard statements | H227 - Combustible liquid. |
| GHS precautionary statements | P210 - Keep away from heat/sparks/open flames/hot surfaces. - No smoking. P280 - Wear protective gloves/eye protection/face protection. P370 + P378 - In case of fire: Use water spray (fog), foam, dry powder or carbon dioxide for extinction. P403 + P235 - Store in a well-ventilated place. Keep cool. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations. |

Other hazards

Splash contact of ethanol with the eye causes immediate stinging and burning. Consumption of ethanol may cause CNS depression, liver toxicity and adverse fetal effects when ingested by pregnant women, but this is not applicable with normal use of the product.

Note

This product component (mixture) is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

| <u>Ingredient</u> | <u>CAS #</u> | <u>EINECS/ ELINCS#</u> | <u>Amount</u> | <u>GHS Classification</u> |
|-------------------|--------------|----------------------------|---------------|---------------------------|
| Ethanol | 64-17-5 | 200-578-6 | 20 % | FL2: H225 |

Note

The ingredient(s) listed above are considered hazardous. Ethanol, ethyl alcohol, and dehydrated alcohol are synonyms for the same chemical compound. The remaining component is propylene glycol (80%), which is not considered hazardous. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

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| Immediate Medical Attention Needed | Yes |
| Eye Contact | If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor. |

SECTION 4 - FIRST AID MEASURES ...continued

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| Skin Contact | Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor. |
| Inhalation | Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor. |
| Ingestion | Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor. |
| Protection of first aid responders | See Section 8 for Exposure Controls/Personal Protection recommendations. |
| Most important symptoms and effects, both acute and delayed | See Sections 2 and 11. |
| Indication of immediate medical attention and special treatment needed, if necessary | Direct contact may cause eye and/or skin irritation. Treat symptomatically and supportively. |

SECTION 5 - FIREFIGHTING MEASURES

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| Extinguishing media | Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials. |
| Specific hazards arising from the substance or mixture | No information identified. |
| Flammability/Explosivity | Flammable. Keep away from heat, sparks and flame. Vapors are heavier than air and may flow along surfaces to remote ignition sources and flashback. |
| Advice for firefighters | In case of a fire, keep containers cool with water and remove from fire area. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Wash all equipment thoroughly after use. |

SECTION 6 - ACCIDENTAL RELEASE MEASURES

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| Personal precautions, protective equipment and emergency procedures | Remove ignition sources. If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe mist/vapors/spray. |
| Environmental precautions | Do not empty into drains. Avoid release to the environment. |

SECTION 6 - ACCIDENTAL RELEASE MEASURES ...continued

| | |
|---|---|
| Methods and material for containment and cleaning up | If vials are opened, crushed or broken, or if handling bulk mixture: DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice. |
| Reference to other sections | See Sections 8 and 13 for more information. |

SECTION 7 - HANDLING AND STORAGE

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| Precautions for safe handling | If vials are opened, crushed or broken, drug substance may be released. Keep away from heat, sparks and open flames. Keep container closed. Use only with adequate ventilation. Avoid contact with skin, mouth, eyes and other mucous membranes. |
| Conditions for safe storage including any incompatibilities | Store at controlled room temperature (<30 °C), in a dry, well-ventilated space away from incompatible materials. Keep away from children. Keep vials in carton, upright and tightly closed. Store locked up. |
| Specific end use(s) | No information identified. |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note Dispose of broken vials in a sharps container.

**Control Parameters/
Occupational Exposure
Limit Values**

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|-----------------|-----------------|--|------------|
| Ethanol | ACGIH, NIOSH | TWA-8 HR | 1000 ppm |
| | NIOSH | IDLH (Immediately dangerous to life or health) | 3300 ppm |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

**Control Parameters/
Occupational Exposure
Limit Values**

...continued

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|-----------------|--|-------------------|------------------------|
| | Austria, Belgium, Denmark, Estonia, Finland, France, Greece, Ireland, Portugal, Romania, Slovenia, Spain, United Kingdom, Mexico, Singapore | TWA-8 HR | 1000 ppm |
| | Austria | STEL (3 x 60 min) | 2000 ppm |
| | Bulgaria, Czech Republic, Latvia | TWA-8 HR | 1000 mg/m ³ |
| | Czech Republic | Ceiling | 3000 mg/m ³ |
| | Estonia, Lithuania, Sweden | STEL | 1000 ppm |
| | Estonia, Germany, Lithuania, Netherlands, Slovak Republic, Sweden | TWA-8 HR | 500 ppm |
| | Finland | STEL | 1300 ppm |
| | France, Romania | STEL | 5000 ppm |
| | Germany, Lithuania | Ceiling | 1000 ppm |
| | Hungary | STEL | 7600 mg/m ³ |
| | Hungary, Poland | TWA-8 HR | 1900 mg/m ³ |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

**Control Parameters/
Occupational Exposure
Limit Values**

...continued

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|-----------------|-----------------|-------------|------------------------|
| | Slovak Republic | Ceiling | 1920 mg/m ³ |
| | Slovenia | STEL | 4000 ppm |
| | United Kingdom | STEL | 3000 ppm |
| | Brazil | TWA-8 HR | 780 ppm |

Exposure/Engineering controls

If vials are opened/crushed/broken: Control exposures to below the OEL. Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for aerosols.

Respiratory protection

If vials are opened/crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine handling tasks, an approved and properly worn powered air-purifying respirator equipped with appropriate HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection

Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

Eye/face protection

Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

Environmental Exposure Controls

Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

Other protective measures Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

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|---|---|
| Appearance | Liquid, packaged in glass vial |
| Color | Clear |
| Odor | Characteristic alcohol odor |
| Odor threshold | No information identified. |
| pH | No information identified. |
| Melting point/ freezing point | -59°C (100% propylene glycol) |
| Initial boiling point and boiling range | ~78°C (100% ethanol); 188°C (100% propylene glycol) |
| Flash point | 36 °C (20% ethanol) |
| Evaporation rate | No information identified. |
| Flammability (solid, gas) | Not applicable. |
| Upper/lower flammability or explosive limits | LEL - 3.3%; UEL - 19% (100% ethanol) |
| Vapor pressure | ~59 mm Hg @ 20°C (100% ethanol); 0.13 mm Hg at 25°C (100% propylene glycol) |
| Vapor density | 1.59 (100% ethanol) |
| Relative density | No information identified. |
| Water solubility | Soluble in water |
| Solvent solubility | No information identified. |
| Partition coefficient (<i>n</i>-octanol/water) | ~0.32 (100% ethanol); -0.92 (propylene glycol) |
| Auto-ignition temperature | No information identified. |

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued

Decomposition temperature No information identified.

Viscosity No information identified.

Explosive properties No information identified.

Oxidizing properties No information identified.

Other information

Molecular formula Not applicable (Mixture)

Molecular weight Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.

Chemical stability Chemically stable.

Possibility of hazardous reactions No information identified.

Conditions to avoid Avoid contact with heat, sparks, flames or other ignition sources. Avoid extreme temperatures.

Incompatible materials No information identified.

Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **The following data describe the toxic properties of ethanol.**

Information on toxicological effects

Route of entry May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

| <u>Compound</u> | <u>Type</u> | <u>Route</u> | <u>Species</u> | <u>Dose</u> |
|-----------------|------------------|--------------|----------------|------------------------------|
| Ethanol | LD ₅₀ | Oral | Rat | 7060 mg/kg |
| | LD ₅₀ | Oral | Mouse | 3400 mg/kg |
| | LC ₅₀ | Inhalation | Rat | 20000 ppm/10 hours |
| | LC ₅₀ | Inhalation | Mouse | 39 g/m ³ /4 hours |

Irritation/Corrosion Ethanol is a skin and eye irritant in animals.

Sensitization Not a skin or respiratory sensitizer.

STOT-single exposure Exposure to large quantities of ethanol can cause nervous system depression.

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

| | |
|--|---|
| STOT-repeated exposure/Repeat-dose toxicity | No data available. |
| Reproductive toxicity | No data available. |
| Developmental toxicity | Consumption of large quantities of ethanol during pregnancy can cause adverse developmental effects in offspring ("fetal alcohol syndrome"), but this is not applicable with normal use of this product. |
| Genotoxicity | Ethanol was positive in a number of genotoxicity assays. These effects may be due to a metabolite, acetaldehyde. |
| Carcinogenicity | Consumption of alcohol is listed as a group I IARC carcinogen (carcinogenic to humans). Ethanol is considered a confirmed animal carcinogen with unknown relevance to humans by ACGIH. No other components of the product present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen. |
| Aspiration hazard | No data available. |
| Human health data | See Section 2 - "Other hazards" |

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

| <u>Compound</u> | <u>Type</u> | <u>Species</u> | <u>Concentration</u> |
|-----------------|----------------------------|----------------------------|---------------------------|
| Ethanol | LC ₅₀ /96h | Rainbow trout | 12900 mg/L (flow through) |
| | LC ₅₀ /96h | Fathead minnow | 15000 mg/L |
| | EC ₅₀ /48h | Daphnia magna | 9268 mg/L |
| | EC ₅₀ /5-30 min | Photobacterium phosphoreum | ~35000 mg/L |

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| Persistence and Degradability | Ethanol is readily biodegradable under aerobic and anaerobic conditions. |
| Bioaccumulative potential | No data identified. |
| Mobility in soil | No data identified. |
| Results of PBT and vPvB assessment | Not performed. |
| Other adverse effects | No data identified. |
| Note | Releases to the environment should be avoided. |

SECTION 13 - DISPOSAL CONSIDERATIONS

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|--------------------------------|---|
| Waste treatment methods | Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, <i>e.g.</i> , appropriately permitted municipal or onsite wastewater treatment facility. |
|--------------------------------|---|

SECTION 14 - TRANSPORT INFORMATION

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| Note | The following applies to product packaged for distribution in shipping containers (combination packaging) weighing 30 kg or less. May be eligible for shipment as an excepted quantity. May be eligible for shipment as a consumer commodity (ID8000, Class 9); refer to instruction Y963. |
| Transport | Packaged product contains two components (vials) which may be regulated for transportation as a hazardous material/dangerous good. Transport information for the diluent solution is as per Vial #2; transport information for packaged product is as per Vials #1 and #2. |
| UN number | Vial #1: UN2811 Vial #2: UN1170 |
| UN proper shipping name | Vial #1: Toxic solid, organic, n.o.s. (contains romidepsin) Vial #2: Ethyl alcohol solution |
| Transport hazard classes and packing group | Vial #1: Hazard Class - 6.1; Packing Group III Vial #2: Hazard Class - 3; Packing Group III |
| Environmental hazards | Based on the available data, this product is not regulated as an environmental hazard or a marine pollutant. |
| Special precautions for users | Avoid release to the environment. |
| Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code | Not applicable. |

SECTION 15 - REGULATORY INFORMATION

| | |
|---|--|
| Safety, health and environmental regulations/legislation specific for the substance or mixture | This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information. |
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SECTION 15 - REGULATORY INFORMATION ...continued

| | |
|-----------------------------------|--|
| Chemical safety assessment | Not conducted. |
| TSCA status | Ethanol and propylene glycol are both listed in the TSCA 8(b) Inventory. |
| SARA section 313 | Ethanol is listed under SARA 313; propylene glycol is not listed. |
| California proposition 65 | Ethyl alcohol as contained in alcoholic beverages (and consumed) is listed as a reproductive toxicant, but this is not applicable with normal use of this product. |
| Additional information | No other information identified. |

SECTION 16 - OTHER INFORMATION

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|---|---|
| Full text of H phrases and GHS classifications | FL2 - Flammable Liquid Category 2. H225 - Highly flammable liquid and vapor. H227 - Combustible liquid. |
| Sources of data | Information from published literature and internal company data. |
| Abbreviations | ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System |
| Issue Date | 23 April 2018 |
| Revisions | Updated address in Section 1 |

SECTION 16 - OTHER INFORMATION ...continued

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a potent pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.