1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Vorinostat Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 50 Tuas West Drive
Singapore - Singapore 638408
Telephone : 908-740-4000
Emergency telephone number : 65 6697 2111 (24/7/365)
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

2. HAZARDS IDENTIFICATION

GHS Classification
Germ cell mutagenicity : Category 2
Reproductive toxicity : Category 1B
Specific target organ toxicity - repeated exposure (Oral) : Category 1 (Blood, thymus gland, Bone marrow, spleen, Gastrointestinal tract)
Short-term (acute) aquatic hazard : Category 1
Long-term (chronic) aquatic hazard : Category 1

GHS label elements
Hazard pictograms : 

Signal word : Danger
Hazard statements : H341 Suspected of causing genetic defects. H360FD May damage fertility. May damage the unborn child. H372 Causes damage to organs (Blood, thymus gland, Bone marrow, spleen, Gastrointestinal tract) through prolonged or repeated exposure if swallowed. H410 Very toxic to aquatic life with long lasting effects.
Precautionary statements:

**Prevention:**
- P201 Obtain special instructions before use.
- P202 Do not handle until all safety precautions have been read and understood.
- P260 Do not breathe dust.
- P264 Wash skin thoroughly after handling.
- P270 Do not eat, drink or smoke when using this product.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/protective clothing/ eye protection/ face protection.

**Response:**
- P308 + P313 IF exposed or concerned: Get medical advice/attention.
- P391 Collect spillage.

**Storage:**
- P405 Store locked up.

**Disposal:**
- P501 Dispose of contents/container to an approved waste disposal plant.

**Other hazards which do not result in classification**

Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vorinostat</td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Vorinostat</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

**General advice:**
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

**If inhaled:**
If inhaled, remove to fresh air.
Get medical attention.

**In case of skin contact:**
In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.
### 5. FIREFIGHTING MEASURES

<table>
<thead>
<tr>
<th>Suitable extinguishing media</th>
<th>Water spray</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcohol-resistant foam</td>
</tr>
<tr>
<td></td>
<td>Carbon dioxide (CO2)</td>
</tr>
<tr>
<td></td>
<td>Dry chemical</td>
</tr>
<tr>
<td>Unsuitable extinguishing media</td>
<td>None known</td>
</tr>
<tr>
<td>Specific hazards during firefighting</td>
<td>Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. Exposure to combustion products may be a hazard to health.</td>
</tr>
<tr>
<td>Hazardous combustion products</td>
<td>Carbon oxides</td>
</tr>
<tr>
<td>Specific extinguishing methods</td>
<td>Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.</td>
</tr>
<tr>
<td>Special protective equipment for firefighters</td>
<td>In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.</td>
</tr>
</tbody>
</table>

### 6. ACCIDENTAL RELEASE MEASURES

| Personal precautions, protective equipment and emergency procedures | Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations. |
| Environmental precautions | Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained. |
| Methods and materials for | Sweep up or vacuum up spillage and collect in suitable con- |
7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Avoid contact with eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage: Keep in properly labelled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vorinostat</td>
<td>149647-78-9</td>
<td>TWA</td>
<td>5 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>50 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
</tbody>
</table>
Engineering measures: Minimize workplace exposure concentrations. Apply measures to prevent dust explosions. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). If sufficient ventilation is unavailable, use with local exhaust ventilation.

Personal protective equipment

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type

Hand protection: Chemical-resistant gloves

Eye protection: Wear the following personal protective equipment: Safety goggles

Skin and body protection: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder

Colour: No data available

Odour: odourless

Odour Threshold: No data available

pH: No data available
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td></td>
</tr>
<tr>
<td>Viscosity, dynamic</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
<tr>
<td>Particle size</td>
<td>No data available</td>
</tr>
</tbody>
</table>

### 10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not classified as a reactivity hazard.</td>
</tr>
<tr>
<td>Chemical stability</td>
<td>Stable under normal conditions.</td>
</tr>
<tr>
<td>Possibility of hazardous reac-</td>
<td>May form explosive dust-air mixture during processing, han-</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

Vorinostat Formulation

Conditions to avoid:
- Heat, flames and sparks.
- Avoid dust formation.

Incompatible materials:
- Oxidizing agents

Hazardous decomposition products:
- No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Components:

Vorinostat:
- Acute oral toxicity:
  - LD50 (Mouse): > 2,000 mg/kg
  - LD50 (Rat): > 750 mg/kg
- Acute toxicity (other routes of administration):
  - LDLo (Mouse): 1,250 mg/kg
  - Application Route: Intravenous
  - Exposure time: 4 h

Cellulose:
- Acute oral toxicity:
  - LD50 (Rat): > 5,000 mg/kg
- Acute inhalation toxicity:
  - LC50 (Rat): > 5.8 mg/l
  - Exposure time: 4 h
  - Test atmosphere: dust/mist
- Acute dermal toxicity:
  - LD50 (Rabbit): > 2,000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:

Vorinostat:
- Species: Rabbit
- Result: No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.
Components:

Vorinostat:
Species: Bovine cornea
Result: No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Vorinostat:
Test Type: Local lymph node assay (LLNA)
Exposure routes: Skin contact
Species: Mouse
Result: Not a skin sensitizer.

Germ cell mutagenicity
Suspected of causing genetic defects.

Components:

Vorinostat:
Genotoxicity in vitro:
Test Type: Bacterial reverse mutation assay (AMES)
Result: positive
Test Type: Chromosome aberration test in vitro
Test system: Chinese hamster ovary cells
Result: positive
Test Type: Chromosome aberration test in vitro
Test system: Human lymphocytes
Result: negative

Genotoxicity in vivo:
Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Oral
Result: positive

Germ cell mutagenicity - Assessment:
Positive result(s) from in vivo mammalian somatic cell mutagenicity tests.

Cellulose:
Genotoxicity in vitro:
Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: In vitro mammalian cell gene mutation test
Result: negative
Genotoxicity in vivo: Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

Reproductive toxicity
May damage fertility. May damage the unborn child.

Components:

Vorinostat:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, female
Application Route: Oral
Fertility: LOAEL: 15 mg/kg body weight
Result: Preimplantation loss, Increased resorptions.

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 50 mg/kg body weight
Result: positive

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 15 mg/kg body weight
Result: positive

Effects on foetal development: Test Type: Embryo-foetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 150 mg/kg body weight
Result: Embryotoxic effects.
**Test Type:** Embryo-foetal development  
**Species:** Rabbit  
**Application Route:** Oral  
**Developmental Toxicity:** NOAEL: 50 mg/kg body weight  
**Result:** Embryotoxic effects.

**Test Type:** Embryo-foetal development  
**Species:** Rabbit  
**Application Route:** Oral  
**Developmental Toxicity:** LOAEL: 15 mg/kg body weight  
**Result:** Malformations were observed.

**Reproductive toxicity - Assessment:**  
Clear evidence of adverse effects on sexual function and fertility, based on animal experiments., Clear evidence of adverse effects on development, based on animal experiments.

**Cellulose:**  
**Effects on fertility:**  
**Species:** Rat  
**Application Route:** Ingestion  
**Result:** negative

**Effects on foetal development:**  
**Species:** Rat  
**Application Route:** Ingestion  
**Result:** negative

**STOT - single exposure**  
Not classified based on available information.

**STOT - repeated exposure**  
Causes damage to organs (Blood, thymus gland, Bone marrow, spleen, Gastrointestinal tract) through prolonged or repeated exposure if swallowed.

**Components:**

**Vorinostat:**  
**Exposure routes:** Ingestion  
**Target Organs:** Blood, thymus gland, Bone marrow, spleen, Gastrointestinal tract  
**Assessment:** Causes damage to organs through prolonged or repeated exposure.

**Repeated dose toxicity**

**Components:**

**Vorinostat:**  
**Species:** Rat  
**LOAEL:** 20 mg/kg  
**Application Route:** Oral  
**Exposure time:** 6 Months  
**Target Organs:** Blood, thymus gland, Bone marrow, spleen
Species: Dog
NOAEL: 60 mg/kg
LOAEL: 160 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Gastrointestinal tract

Species: Dog
NOAEL: 40 mg/kg
LOAEL: 100 mg/kg
Application Route: Oral
Exposure time: 4 Weeks
Target Organs: Blood

**Cellulose:**
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

**Aspiration toxicity**
Not classified based on available information.

**Experience with human exposure**

**Components:**

**Vorinostat:**
Ingestion
Symptoms: Diarrhoea, Fatigue, Nausea, anorexia

### 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Vorinostat:**
Toxicity to fish
LC50 (Pimephales promelas (fathead minnow)): > 10 mg/l
Exposure time: 96 h
LC50 (Cyprinodon variegatus (sheepshead minnow)): > 10 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates
EC50 (Daphnia magna (Water flea)): > 10 mg/l
Exposure time: 48 h
EC50 (Americamysis): 7.4 mg/l
Exposure time: 96 h

Toxicity to algae/aquatic plants
EC50 (Pseudokirchneriella subcapitata (green algae)): 0.183 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 201
NOEC (Pseudokirchneriella subcapitata (green algae)): 0.011 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 201

M-Factor (Acute aquatic toxicity):
Toxicity to fish (Chronic toxicity):

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

M-Factor (Chronic aquatic toxicity):
Toxicity to microorganisms:

Cellulose:
Toxicity to fish:

Persistence and degradability

Components:
Vorinostat:
Biodegradability:
Result: Not readily biodegradable.
Biodegradation: 39.5%
Exposure time: 28 d
Method: OECD Test Guideline 314

Cellulose:
Biodegradability:
Result: Readily biodegradable.

Bioaccumulative potential

Components:
Vorinostat:
Partition coefficient: n-octanol/water:
log Pow: 1.42

Mobility in soil

Components:
Vorinostat:
Distribution among environment:
log Koc: 3.37
ment compartments

Other adverse effects
No data available

13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues : Dispose of in accordance with local regulations.
Contaminated packaging : Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Vorinostat)
Class : 9
Packing group : III
Labels : 9

IATA-DGR
UN/ID No. : UN 3077
Proper shipping name : Environmentally hazardous substance, solid, n.o.s. (Vorinostat)
Class : 9
Packing group : III
Labels : Miscellaneous
Packing instruction (cargo aircraft) : 956
Packing instruction (passenger aircraft) : 956
Environmentally hazardous : yes

IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Vorinostat)
Class : 9
Packing group : III
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data
SAFETY DATA SHEET

Vorinostat Formulation

Version 3.9 Revision Date: 09/13/2019 SDS Number: 42861-00013 Date of last issue: 24.04.2019 Date of first issue: 06.01.2015

Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

15. REGULATORY INFORMATION

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

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

The components of this product are reported in the following inventories:

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>not determined</td>
</tr>
<tr>
<td>DSL</td>
<td>not determined</td>
</tr>
<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Further information


Date format: dd.mm.yyyy

Full text of other abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH / TWA</td>
<td>USA. ACGIH Threshold Limit Values (TLV)</td>
</tr>
<tr>
<td>SG OEL</td>
<td>Singapore. Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances</td>
</tr>
</tbody>
</table>
| AICS         | Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and
## Equipment of Ships carrying Dangerous Chemicals in Bulk

IC50 - Half maximal inhibitory concentration

ICAO - International Civil Aviation Organization

IECSC - Inventory of Existing Chemical Substances in China

IMDG - International Maritime Dangerous Goods

IMO - International Maritime Organization

ISHL - Industrial Safety and Health Law (Japan)

ISO - International Organization for Standardization

KECI - Korea Existing Chemicals Inventory

LC50 - Lethal Concentration to 50% of a test population

LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose)

MARPOL - International Convention for the Prevention of Pollution from Ships

n.o.s. - Not Otherwise Specified

Nch - Chilean Norm

NO(A)EC - No Observed (Adverse) Effect Concentration

NO(A)EL - No Observed (Adverse) Effect Level

NOELR - No Observable Effect Loading Rate

NOM - Official Mexican Norm

NTP - National Toxicology Program

NZIoC - New Zealand Inventory of Chemicals

OECD - Organization for Economic Co-operation and Development

OPPTS - Office of Chemical Safety and Pollution Prevention

PBT - Persistent, Bioaccumulative and Toxic substance

PICCS - Philippines Inventory of Chemicals and Chemical Substances

(Q)SAR - (Quantitative) Structure Activity Relationship


SADT - Self-Accelerating Decomposition Temperature

SDS - Safety Data Sheet

TCSI - Taiwan Chemical Substance Inventory

TDG - Transportation of Dangerous Goods

TSCA - Toxic Substances Control Act (United States)

UN - United Nations

UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods

vPvB - Very Persistent and Very Bioaccumulative

WHMIS - Workplace Hazardous Materials Information System

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

SG / EN