SAFETY DATA SHEET
Vorinostat Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Vorinostat Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone : 908-740-4000
Emergency telephone : 55 19 3758 2000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Acute toxicity (Oral) : Category 5
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 in accordance with ABNT NBR 14725 Standard
Hazard pictograms :

Signal Word : Danger
Hazard Statements : H303 May be harmful if swallowed.
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.
- P260 Do not breathe dust.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/protective clothing/eye protection/face protection.

**Response:**
- P312 Call a POISON CENTER/doctor if you feel unwell.
- P391 Collect spillage.

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.

### SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

**Substance / Mixture:** Mixture

**Components**

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vorinostat</td>
<td>149647-78-9</td>
<td>Acute toxicity (Oral), Germ cell mutagenicity, Reproductive toxicity, Specific target organ toxicity - repeated exposure (Oral) (Blood, thymus gland, Bone marrow, spleen, Gastrointestinal tract), Short-term (acute) aquatic hazard, Long-term (chronic) aquatic hazard</td>
<td>&gt;= 50 &lt; 70</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td></td>
<td>&gt;= 20 &lt; 30</td>
</tr>
</tbody>
</table>

### SECTION 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.

In case of eye contact: If in eyes, rinse well with water. Get medical attention if irritation develops and persists.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: May be harmful if swallowed. Suspected of causing genetic defects. May damage fertility. May damage the unborn child. Causes damage to organs through prolonged or repeated exposure if swallowed. Contact with dust can cause mechanical irritation or drying of the skin. Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

Specific hazards during fire fighting: 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.

Hazardous combustion products: Carbon oxides

Specific extinguishing methods: 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.

Special protective equipment for fire-fighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 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 containment and cleaning up
Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

---

### SECTION 7. HANDLING AND STORAGE

<table>
<thead>
<tr>
<th>Technical measures</th>
<th>Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local/Total ventilation</td>
<td>If sufficient ventilation is unavailable, use with local exhaust ventilation.</td>
</tr>
<tr>
<td>Advice on safe handling</td>
<td>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.</td>
</tr>
<tr>
<td>Hygiene measures</td>
<td>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.</td>
</tr>
</tbody>
</table>

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4 / 15
Materials to avoid: Do not store with the following product types:
- Strong oxidizing agents
- Organic peroxides
- Explosives
- Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

**Ingredients 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>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</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

**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.).
SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder
Color : No data available
Odor : odorless
Odor Threshold : No data available
pH : No data available
Melting point/freezing point : No data available
Initial boiling point and boiling range : No data available
Flash point : No data available
Evaporation rate : No data available
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
Flammability (liquids) : No data available
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Vapor pressure : No data available
Relative vapor density : No data available
Density : No data available
Solubility(ies)
  Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
  Viscosity, dynamic : No data available
  Viscosity, kinematic : No data available
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
SAFETY DATA SHEET
Vorinostat Formulation

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid : Heat, flames and sparks. Avoid dust formation.
Incompatible materials : Oxidizing agents
Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

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

Acute toxicity
May be harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 3.788 mg/kg
Method: Calculation method

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 sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

**Components:**

**Vorinostat:**
Test Type: Local lymph node assay (LLNA)
Routes of exposure: 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
## SAFETY DATA SHEET

### Vorinostat Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2</td>
<td>09/13/2019</td>
<td>42845-00013</td>
<td>24.04.2019</td>
<td>06.01.2015</td>
</tr>
</tbody>
</table>

**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.

- **Test Type:** Fertility/early embryonic development
  - **Species:** Rat, male
  - **Application Route:** Oral
  - **Fertility:** NOAEL: 150 mg/kg body weight
  - **Result:** No effects on fertility.

#### Effects on fetal development

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

- **Test Type:** Embryo-fetal development
## Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 15 mg/kg body weight
Result: positive

Test Type: Embry-o-fetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 150 mg/kg body weight
Result: Embryotoxic effects.

Test Type: Embry-o-fetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: NOAEL: 50 mg/kg body weight
Result: Embryotoxic effects.

Test Type: Embry-o-fetal 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:

<table>
<thead>
<tr>
<th>Effects on fertility</th>
<th>Test Type: One-generation reproduction toxicity study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects on fetal development</th>
<th>Test Type: Fertility/early embryonic development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species: Rat</td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>

### 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:
- **Routes of exposure**: 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: Diarrhea, Fatigue, Nausea, anorexia

SECTION 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):
- 1

Toxicity to fish (Chronic toxicity):
- NOEC (Pimephales promelas (fathead minnow)): 1,5 mg/l
  Exposure time: 33 d
  Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
- NOEC (Daphnia magna (Water flea)): 0,15 mg/l
  Exposure time: 21 d
  Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity):
- 1

Toxicity to microorganisms:
- EC50: > 1.000 mg/l
  Exposure time: 3 h
  Test Type: Respiration inhibition

Cellulose:
Toxicity to fish:
- LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
  Exposure time: 48 h
  Remarks: Based on data from similar materials

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 environmental compartments : log Koc: 3,37

Other adverse effects
No data available

SECTION 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.

SECTION 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.

Domestic regulation

ANTT
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Vorinostat)
Class : 9
Packing group : III
Labels : 9
Hazard Identification Number : 90

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

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable

Brazil. Ordinance No. 1274 on the control and monitoring of chemicals. : Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Further information
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.

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