1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Vorinostat Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Briahnager - Off Pune Nagar Road Wagholi - Pune - India  412 207
Telephone : 908-740-4000
Emergency telephone number : 1-908-423-6000
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

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
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
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:  
P203 Obtain, read and follow all safety instructions before use.  
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:  
P301 + P317 IF SWALLOWED: Get medical help.  
P318 IF exposed or concerned, get medical advice.  
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

Substance / Mixture:  
Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vorinostat</td>
<td>149647-78-9</td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 20 - &lt; 30</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.

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.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: 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 firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).
Environmental precautions:
- Avoid release to the environment.
- 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.

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 with 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.
- Wash skin thoroughly after handling.
- 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.
- Do not eat, drink or smoke when using this product.
- 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>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

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

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
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>odourless</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<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>
</tbody>
</table>
Vorinostat Formulation

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.

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 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: Positive result(s) from in vivo mammalian somatic cell muta-
Assessment geneicity 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 foetal development:
- Test Type: Embryo-foetal development
  - Species: Rat
  - Application Route: Oral
  - Developmental Toxicity: LOAEL: 50 mg/kg body weight
  - Result: positive

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

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: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development: Test Type: Fertility/early embryonic 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): 1

Toxicity to microorganisms: EC50: > 1,000 mg/l
   Exposure time: 3 h
   Test Type: Respiration inhibition

Toxicity to fish (Chronic toxicity): NOEC: 1.5 mg/l
   Exposure time: 33 d
   Species: Pimephales promelas (fathead minnow)
   Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 0.15 mg/l
   Exposure time: 21 d
   Species: Daphnia magna (Water flea)
   Method: OECD Test Guideline 211

M-Factor (Chronic aquatic toxicity): 1

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: 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

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
SAFETY DATA SHEET

Vorinostat Formulation

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 IMO instruments
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 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

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

16. OTHER INFORMATION

Further information

Date format: dd.mm.yyyy

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

AIIIC - Australian Inventory of Industrial Chemicals; 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;
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.

IN / EN