SAFETY DATA SHEET

Vorinostat Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 30.09.2023
5.0	06.04.2024	42861-00022	Date of first issue: 06.01.2015

Section 1: Identification

Product identifier : Vorinostat Formulation

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical
Restrictions on use : Not applicable

Manufacturer or supplier's details

Company : MSD

Address : 50 Tuas West Drive
Singapore - Singapore 638408

Telephone : +1-908-740-4000

Emergency telephone number : 65 6697 2111 (24/7/365)

E-mail address : EHSDATASTEWARD@msd.com

Section 2: Hazard identification

Classification of the substance or mixture

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, including precautionary statements

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/ hearing 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.

Section 3: Composition/information on ingredients

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)
Vorinostat	149647-78-9	>= 50 -< 70
Cellulose	9004-34-6	>= 20 -< 30

Section 4: First-aid measures

Description of necessary 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

Risks	:	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).

Indication of any immediate medical attention and special treatment needed

Treatment	:	Treat symptomatically and supportively.

Section 5: Fire-fighting measures

Extinguishing media

Suitable extinguishing media	:	Water spray Alcohol-resistant foam Carbon dioxide (CO2) Dry chemical
Unsuitable extinguishing media	:	None known.

Special hazards arising from the substance or mixture

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 Metal oxides

Special protective actions for fire-fighters

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

Section 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures

Personal precautions : Use personal protective equipment.
Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions

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

Methods for 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

Precautions for safe handling

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.

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.

Conditions for safe storage, including any incompatibilities

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

Section 8: Exposure controls/personal protection

Control parameters

Occupational Exposure Limits

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Vorinostat	149647-78-9	TWA	5 µg/m3	Internal
		Wipe limit	50 µg/100 cm²	Internal
Cellulose	9004-34-6	PEL (long term)	10 mg/m3	SG OEL
		TWA	10 mg/m3	ACGIH

Appropriate engineering control 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.

Individual protection measures, such as personal protective equipment (PPE)

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

Skin 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).
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.

Section 9: Physical and chemical properties

Appearance	:	powder
Colour	:	No data available
Odour	:	odourless
Odour 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

Vapour pressure	:	No data available
Relative vapour density	:	No data available
Density	:	No data available
Solubility(ies)		
Water solubility	:	No data available
Partition coefficient: n-octanol/water	:	No data available
Auto-ignition 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.
Molecular weight	:	No data available
Particle characteristics		
Particle size	:	No data available

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

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. 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

Section 12: Ecological information

Toxicity

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	:	Do not dispose of waste into sewer. 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
UN proper shipping name	:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Vorinostat)
Transport hazard class(es)	:	9
Packing group	:	III
Labels	:	9
Environmental hazards	:	yes

IATA-DGR

UN/ID No.	:	UN 3077
UN proper shipping name	:	Environmentally hazardous substance, solid, n.o.s. (Vorinostat)
Transport hazard class(es)	:	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)
Transport hazard class(es)	:	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.

Section 15: Regulatory information

Safety, health and environmental regulations specific for the product in question

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:

AICS	:	not determined
DSL	:	not determined
IECSC	:	not determined

Section 16: Other information

Revision Date	:	06.04.2024

Further information

Sources of key data used to compile the Safety Data Sheet	:	Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, http://echa.europa.eu/

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Date format	:	dd.mm.yyyy

Full text of other abbreviations

ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
SG OEL	:	Singapore. Workplace Safety and Health (General Provisions) Regulations - First Schedule Permissible Exposure Limits of Toxic Substances.
ACGIH / TWA	:	8-hour, time-weighted average

SG OEL / PEL (long term) : Permissible Exposure Level (PEL) Long Term

AIIC - 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; 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 Organisation 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; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TECI - Thailand Existing Chemicals Inventory; 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