SAFETY DATA SHEET

Aprepitant Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 26.09.2023
6.2	24.01.2024	20609-00026	Date of first issue: 09.10.2014

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Aprepitant Formulation

Manufacturer or supplier's details

Company name of supplier : MSD
Address : 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical
Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Prostate, Testis)

GHS label elements

Hazard pictograms :

Signal Word : Warning

Hazard Statements : H373 May cause damage to organs (Prostate, Testis) through prolonged or repeated exposure if swallowed.

Precautionary Statements :

Prevention:

P260 Do not breathe dust.

Response:

P314 Get medical advice/ attention if you feel unwell.

Disposal:

P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards

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)
Aprepitant	170729-80-3	>= 30 -< 50
Sucrose	57-50-1	>= 30 -< 50
Cellulose	9004-34-6	>= 10 -< 20

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 if symptoms occur.

In case of skin contact : Wash with water and soap.
Get medical attention if symptoms occur.

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 if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed : May cause 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
Fluorine compounds
Nitrogen oxides (NOx)

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 (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.

SECTION 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	:	Use only with adequate ventilation.
Advice on safe handling	:	Do not breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment 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.
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.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage : Keep in properly labeled containers.
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

Ingredients with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Aprepitant	170729-80-3	TWA	0.2 mg/m3 (OEB 2)	Internal
Sucrose	57-50-1	VLE-PPT	10 mg/m³	NOM-010-STPS-2014
		TWA	10 mg/m³	ACGIH
Cellulose	9004-34-6	VLE-PPT	10 mg/m³	NOM-010-STPS-2014
		TWA	10 mg/m³	ACGIH

Engineering measures : Use feasible engineering controls to minimize exposure to compound.
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

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

Eye protection : Wear safety glasses with side shields or goggles.
If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection : Work uniform or laboratory coat.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder

Color : colored

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
Relative 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, kinematic	:	No data available
Explosive properties	:	Not explosive
Oxidizing properties	:	The substance or mixture is not classified as oxidizing.
Molecular weight	:	No data available
Minimum ignition energy	:	< 3 mJ

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:

Aprepitant:

Acute oral toxicity	:	LD50 (Rat): > 2,000 mg/kg LD50 (Mouse): > 2,000 mg/kg
Acute toxicity (other routes of administration)	:	LD50 (Rat): 800 - 2,000 mg/kg Application Route: Intraperitoneal LD50 (Mouse): > 2,000 mg/kg Application Route: Intraperitoneal

Sucrose:

Acute oral toxicity	:	LD50 (Rat): 29,700 mg/kg

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:

Aprepitant:

Species	:	Rabbit
Method	:	Draize Test
Result	:	No skin irritation

Serious eye damage/eye irritation

Not classified based on available information.

Components:

Aprepitant:

Species	:	Rabbit
Result	:	No eye irritation
Method	:	Draize Test

Respiratory or skin sensitization

Skin sensitization

Not classified based on available information.

Respiratory sensitization

Not classified based on available information.

Components:

Aprepitant:

Remarks	:	No data available

Germ cell mutagenicity

Not classified based on available information.

Components:

Aprepitant:

Genotoxicity in vitro	:	Test Type: Ames test Result: negative Test Type: Chromosomal aberration Test system: Chinese hamster ovary cells Result: negative Test Type: Alkaline elution assay Test system: rat hepatocytes Result: negative Test Type: in vitro test Test system: human lymphoblastoid cells Result: negative

Genotoxicity in vivo : Test Type: Micronucleus test
Species: Mouse
Application Route: Oral
Result: negative

Sucrose:

Genotoxicity in vitro : Test Type: In vitro mammalian cell gene mutation test
Result: negative

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:

Aprepitant:

Species	:	Mouse, male
Application Route	:	Oral
Exposure time	:	106 weeks
Dose	:	>=1000 mg/kg body weight
Result	:	positive
Remarks	:	The mechanism or mode of action is not relevant in humans.

Species	:	Mouse, female
Application Route	:	Oral
Exposure time	:	106 weeks
Dose	:	>= 500 mg/kg body weight
Result	:	positive
Remarks	:	The mechanism or mode of action is not relevant in humans.

Species	:	Mouse
Application Route	:	Oral
Exposure time	:	105 weeks
Dose	:	2000 mg/kg body weight
Result	:	positive
Remarks	:	The mechanism or mode of action is not relevant in humans.

Cellulose:

Species : Rat

Application Route	:	Ingestion
Exposure time	:	72 weeks
Result	:	negative

Reproductive toxicity

Not classified based on available information.

Components:

Aprepitant:

Effects on fertility	:	Test Type: Fertility Species: Rat, male and female Fertility: NOAEL: 2,000 mg/kg body weight Result: No effects on fertility.
Effects on fetal development	:	Test Type: Development Species: Rat Application Route: Oral Developmental Toxicity: NOAEL: 2,000 mg/kg body weight Result: No effects on fetal development. Test Type: Development Species: Rabbit Application Route: Oral Developmental Toxicity: NOAEL: 25 mg/kg body weight Result: No effects on fetal development.

Cellulose:

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

May cause damage to organs (Prostate, Testis) through prolonged or repeated exposure if swallowed.

Components:

Aprepitant:

Target Organs	:	Prostate, Testis
Assessment	:	May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Aprepitant:

Species	:	Dog
LOAEL	:	>= 50 mg/kg
Application Route	:	Oral
Exposure time	:	39 Weeks
Target Organs	:	Prostate, Testis

Species	:	Rat
NOAEL	:	125 mg/kg
Application Route	:	Oral
Exposure time	:	27 Weeks
Target Organs	:	Liver, Thyroid

Species	:	Monkey
NOAEL	:	0.240 mg/kg
Application Route	:	Intravenous
Exposure time	:	7 d
Remarks	:	No significant adverse effects were reported

Species	:	Rat, female
LOAEL	:	125 mg/kg
Application Route	:	Oral
Exposure time	:	106 Weeks
Target Organs	:	Kidney

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:

Aprepitant:

Ingestion	:	Symptoms: Headache, Fatigue, hiccups, constipation, anorexia, liver function change, Rash, Nausea, Diarrhea, hypotension

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Aprepitant:

Toxicity to fish	:	LC50 (Pimephales promelas (fathead minnow)): > 0.462 mg/l Exposure time: 96 h Method: OECD Test Guideline 203 Remarks: No toxicity at the limit of solubility.
Toxicity to daphnia and other aquatic invertebrates	:	EC50 (Daphnia magna (Water flea)): > 0.345 mg/l Exposure time: 48 h Method: OECD Test Guideline 202 Remarks: No toxicity at the limit of solubility.
Toxicity to algae/aquatic plants	:	NOEC (Pseudokirchneriella subcapitata (green algae)): 0.184 mg/l Exposure time: 72 h Method: OECD Test Guideline 201 Remarks: No toxicity at the limit of solubility. EC50 (Pseudokirchneriella subcapitata (green algae)): > 0.184 mg/l Exposure time: 72 h Method: OECD Test Guideline 201 Remarks: No toxicity at the limit of solubility.
Toxicity to fish (Chronic toxicity)	:	NOEC (Pimephales promelas (fathead minnow)): 0.195 mg/l Exposure time: 32 d Method: OECD Test Guideline 210
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)	:	NOEC (Daphnia magna (Water flea)): 0.018 mg/l Exposure time: 21 d Method: OECD Test Guideline 211
Toxicity to microorganisms	:	EC50: > 100 mg/l Exposure time: 3 h Test Type: Respiration inhibition Method: OECD Test Guideline 209 Remarks: No toxicity at the limit of solubility.

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:

Aprepitant:

Biodegradability	:	Result: not rapidly degradable Biodegradation: 50 % Exposure time: 66 Days Method: OECD Test Guideline 314

Cellulose:

Biodegradability	:	Result: Readily biodegradable.

Bioaccumulative potential

Components:

Aprepitant:

Bioaccumulation	:	Species: Lepomis macrochirus (Bluegill sunfish) Bioconcentration factor (BCF): 50.1 Method: OECD Test Guideline 305
Partition coefficient: n-octanol/water	:	log Pow: 4.75

Sucrose:

Partition coefficient: n-octanol/water	:	Pow: < 1

Mobility in soil

Components:

Aprepitant:

Distribution among environmental compartments	:	log Koc: 3.10

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
Proper shipping name	:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Aprepitant)
Class	:	9
Packing group	:	III
Labels	:	9
Environmentally hazardous	:	yes

IATA-DGR

UN/ID No.	:	UN 3077
Proper shipping name	:	Environmentally hazardous substance, solid, n.o.s. (Aprepitant)

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. (Aprepitant)
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

NOM-002-SCT

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

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

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills. : Not applicable

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

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

SECTION 16. OTHER INFORMATION

Revision Date	:	24.01.2024
Date format	:	dd.mm.yyyy

Full text of other abbreviations

ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014	:	Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
ACGIH / TWA	:	8-hour, time-weighted average
NOM-010-STPS-2014 / VLE-PPT	:	Time weighted average limit value

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

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

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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