SAFETY DATA SHEET

Aprepitant Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Aprepitant 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

Manufacturer, 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
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Prostate, Testis)
Long-term (chronic) aquatic hazard : Category 1

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.
H410 Very toxic to aquatic life with long lasting effects.

Precautionary statements : Prevention:
P260 Do not breathe dust.
P273 Avoid release to the environment.
Response:
P314 Get medical advice/attention if you feel unwell.
P391 Collect spillage.

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>Aprepitant</td>
<td>170729-80-3</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
<tr>
<td>Sucrose</td>
<td>57-50-1</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 20</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 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.

5. FIREFIGHTING MEASURES

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

None known.

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.

Carbon oxides
Fluorine compounds
Nitrogen oxides (NOx)

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.

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

Use personal protective equipment.
Follow safe handling advice and personal protective equipment recommendations.

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.

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.

Static electricity may accumulate and ignite suspended dust causing an explosion.
Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.
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Version 3.3  Revision Date: 22.10.2019  SDS Number: 20604-00016  Date of last issue: 13.09.2019
Date of first issue: 09.10.2014

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.

Conditions for safe storage:
- Keep in properly labelled containers.
- 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>Sucrose</td>
<td>57-50-1</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Aprepitant</td>
<td>170729-80-3</td>
<td>TWA</td>
<td>0.2 mg/m³ (8-hr TWA)</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:
- Ensure adequate ventilation, especially in confined areas.
- 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).

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 : Skin should be washed after contact.

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

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder

Colour : coloured

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

Relative density : No data available

Density : No data available

Solubility(ies) : No data available
     Water solubility

Partition coefficient: n-octanol/water : No data available
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
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
Method : Draize Test
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:
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
### 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:** $\geq 1000$ 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:** $\geq 500$ 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.

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 foetal development: Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 2,000 mg/kg body weight
Result: No effects on foetal development

Species: Rabbit
Application Route: Oral
Developmental Toxicity: NOAEL: 25 mg/kg body weight
Result: No effects on foetal development

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
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: \( \geq 50 \text{ mg/kg} \)
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: \( \geq 9,000 \text{ mg/kg} \)
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, Diarrhoea, hypotension

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 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

Toxicity to fish (Chronic toxicity): NOEC: 0.195 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 0.018 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211

M-Factor (Chronic aquatic): 1
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Date of first issue: 09.10.2014

toxicity)

**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
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. (Aprepitant)
- Class: 9
- Packing group: III
- Labels: 9

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 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.
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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

- AC-GIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International 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 Tem-
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.