SAFETY DATA SHEET

Aprepitant Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Aprepitant Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Avenida Tanner de Melo, Quadra 10 Lote 4A, Galpão A Parque Industrial Vice Presidente José Alencar Aparecida de Goias – GO, Brazil
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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Prostate, Testis)
Long-term (chronic) aquatic hazard: Category 1

GHS label elements in accordance with ABNT NBR 14725 Standard
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.
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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td>Mixture</td>
<td>Aprepitant</td>
</tr>
<tr>
<td></td>
<td>Sucrose</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice: In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air. Get medical attention 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

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 spills 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.

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

<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>Aprepitant</td>
<td>170729-80-3</td>
<td>TWA</td>
<td>0.2 mg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Sucrose</td>
<td>57-50-1</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</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: Participulates type

Hand protection:
- Material: Chemical-resistant gloves

Remarks:
- Choose gloves to protect hands against chemicals depending on the concentration 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.

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:
**SAFETY DATA SHEET**

**Aprepitant Formulation**

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
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<tr>
<td>4.7</td>
<td>27.08.2021</td>
<td>20589-00020</td>
<td>05.10.2020</td>
<td>09.10.2014</td>
</tr>
</tbody>
</table>

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:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Method</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>Draize Test</td>
<td>No skin irritation</td>
</tr>
</tbody>
</table>

**Serious eye damage/eye irritation**

Not classified based on available information.

**Components:**

**Aprepitant:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Result</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>No eye irritation</td>
<td>Draize Test</td>
</tr>
</tbody>
</table>

**Respiratory or skin sensitization**

**Skin sensitization**

Not classified based on available information.

**Respiratory sensitization**

Not classified based on available information.

**Components:**

**Aprepitant:**

<table>
<thead>
<tr>
<th>Remarks</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No data available</td>
<td></td>
</tr>
</tbody>
</table>

**Germ cell mutagenicity**

Not classified based on available information.

**Components:**

**Aprepitant:**

<table>
<thead>
<tr>
<th>Genotoxicity in vitro</th>
<th>Test Type: Ames test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result: negative</td>
<td></td>
</tr>
</tbody>
</table>
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.

M-Factor (Chronic aquatic toxicity):
- 1

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 : 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

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

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

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
National List of Carcinogenic Agents for Humans: 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**

**Further information**

Sources of key data used to compile the Material Safety Data Sheet:

**Full text of other abbreviations**

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

**Abbreviations used**:
- **AII-C**: 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);
- **EC**: Concentration associated with x% response;
- **EL**: 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**: US 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;
- **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 Sub...
stances 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.

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