SAFETY DATA SHEET

Aprepitant Formulation

Product name: Aprepitant Formulation

Manufacturer or supplier’s details

Company: MSD
Address: 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB
Telephone: 908-740-4000
Emergency telephone: 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

SECTION 2. HAZARDS IDENTIFICATION

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.

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></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

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 and personal protective equipment recommendations.

Environmental precautions: 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.

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.

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 (8-hr TWA)</td>
<td>Internal</td>
</tr>
<tr>
<td>Sucrose</td>
<td>57-50-1</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
</tbody>
</table>

Further information: A4 - Not classifiable as a human carcinogen: Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. In vitro or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories., lung

<table>
<thead>
<tr>
<th>Components</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></td>
</tr>
<tr>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
<td></td>
</tr>
</tbody>
</table>

Further information: Irritation

<table>
<thead>
<tr>
<th>Components</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
<td></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
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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.

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.

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
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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 exposure): LD50 (Rat): 800 - 2.000 mg/kg
administration) 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

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.

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
Argentina. Carcinogenic Substances and Agents Registry : Not applicable

Control of precursors and essential chemicals for the : Not applicable
preparation of drugs.

International Regulations

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

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>not determined</td>
</tr>
<tr>
<td>DSL</td>
<td>not determined</td>
</tr>
<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

SECTION 16. OTHER INFORMATION

Further information


Full text of other abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH</td>
<td>USA. ACGIH Threshold Limit Values (TLV)</td>
</tr>
<tr>
<td>AR OEL</td>
<td>Argentina. Occupational Exposure Limits</td>
</tr>
<tr>
<td>ACGIH / TWA</td>
<td>8-hour, time-weighted average</td>
</tr>
<tr>
<td>AR OEL / CMP</td>
<td>TLV (Threshold Limit Value)</td>
</tr>
</tbody>
</table>

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 Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transporta-
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.