SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier

Trade name : Aprepitant Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against

Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet

Company : MSD
117 16th Road
07033 Halfway house, Midrand, South Africa

Telephone : +27 11 655 3000

Telefax : 908-735-1496

E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number

1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification (REGULATION (EC) No 1272/2008)
Specific target organ toxicity - repeated exposure, Category 2
Long-term (chronic) aquatic hazard, Category 1

H373: May cause damage to organs through prolonged or repeated exposure.
H410: Very toxic to aquatic life with long lasting effects.

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)

Hazard pictograms : 

Signal word : Warning

Hazard statements : 
H373 May cause damage to organs through prolonged or repeated exposure.
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.

Hazardous components which must be listed on the label:

Aprepitant

**2.3 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

#### 3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant</td>
<td>170729-80-3</td>
<td></td>
<td></td>
<td>STOT RE2; H373 Aquatic Chronic1; H410 M-Factor (Chronic aquatic toxicity): 1</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

### SECTION 4: First aid measures

#### 4.1 Description of 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.

**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).

**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.

4.2 Most important symptoms and effects, both acute and delayed

Risks : May cause damage to organs through prolonged or repeated exposure.
        Contact with dust can cause mechanical irritation or drying of the skin.
        Dust contact with the eyes can lead to mechanical irritation.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment : Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

Unsuitable extinguishing media : None known.

5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting : 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)

5.3 Advice for firefighters

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

Specific extinguishing methods : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
                                Use water spray to cool unopened containers.
                                Remove undamaged containers from fire area if it is safe to do so.
                                Evacuate area.
SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures
Personal precautions: Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions
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.

6.3 Methods and material for containment and cleaning up
Methods for cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling
Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.
Local/Total ventilation: 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.
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Date of first issue: 09.10.2014

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.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.
Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)
Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrose</td>
<td>57-50-1</td>
<td>TWA OEL-RL</td>
<td>10 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td>Further information</td>
<td>Recommended Limit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEL OEL-RL</td>
<td>20 mg/m³</td>
<td>ZA OEL</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>Further information</td>
<td>Recommended Limit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA OEL-RL (Respirable dust)</td>
<td>5 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td>Further information</td>
<td>Recommended Limit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA OEL-RL (inhalable dust)</td>
<td>10 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEL OEL-RL (Dust)</td>
<td>20 mg/m³</td>
<td>ZA OEL</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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
Eye protection: Wear the following personal protective equipment:
### Safety goggles

**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.

**Skin and body protection**: Skin should be washed after contact.

**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 (P)

### SECTION 9: Physical and chemical properties

#### 9.1 Information on basic 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.
- **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)
- Water solubility: No data available
- Partition coefficient: n-octanol/water: No data available
- Auto-ignition temperature: No data available
- Decomposition temperature: No data available

Viscosity
- Viscosity, kinematic: No data available

Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.

9.2 Other information
- Flammability (liquids): No data available
- Molecular weight: No data available
- Minimum ignition energy: < 3 mJ
- Particle size: No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of: Inhalation
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

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
- 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 assay
  Test system: human lymphoblastoid cells
  Result: negative

Genotoxicity in vivo:
- Test Type: Micronucleus test
  Species: Mouse
  Application Route: Oral
  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.
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:
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

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs through prolonged or repeated exposure.

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
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<thead>
<tr>
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<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
</table>

- **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

**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

**SECTION 12: Ecological information**

**12.1 Toxicity**

**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
  - **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 toxicity) : 1

12.2 Persistence and degradability

Components:

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

12.3 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

12.4 Mobility in soil

Components:

Aprepitant:
Distribution among environmental compartments : log Koc: 3,10

12.5 Results of PBT and vPvB assessment

Not relevant

12.6 Other adverse effects

No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product : Dispose of in accordance with local regulations.
According to the European Waste Catalogue, Waste Codes
Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities. Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.
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Date of first issue: 09.10.2014

Packing group: III
Classification Code: M7
Hazard Identification Number: 90
Labels: 9
Tunnel restriction code: (-)

RID
Packing group: III
Classification Code: M7
Hazard Identification Number: 90
Labels: 9

IMDG
Packing group: III
Labels: 9
EmS Code: F-A, S-F

IATA (Cargo)
Packing instruction (cargo aircraft): 956
Packing instruction (LQ): Y956
Packing group: III
Labels: Miscellaneous

IATA (Passenger)
Packing instruction (passenger aircraft): 956
Packing instruction (LQ): Y956
Packing group: III
Labels: Miscellaneous

14.5 Environmental hazards

ADN
Environmentally hazardous: yes

ADR
Environmentally hazardous: yes

RID
Environmentally hazardous: yes

IMDG
Marine pollutant: yes

IATA (Passenger)
Environmentally hazardous: yes

IATA (Cargo)
Environmentally hazardous: yes

14.6 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.

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code

Remarks: Not applicable for product as supplied.
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SECTION 15: Regulatory information

15.1 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

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

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

Full text of H-statements

- H373 : May cause damage to organs through prolonged or repeated exposure if swallowed.
- H410 : Very toxic to aquatic life with long lasting effects.

Full text of other abbreviations

- Aquatic Chronic : Long-term (chronic) aquatic hazard
- STOT RE : Specific target organ toxicity - repeated exposure
- ZA OEL : South Africa, Hazardous Chemical Substances Regulations, Occupational Exposure Limits
- ZA OEL / TWA OEL-RL : Long term occupational exposure limits - recommended limit
- ZA OEL / STEL OEL-RL : Short term occupational exposure limits - recommended limit

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; 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; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance 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

Further information

Classification of the mixture: Classification procedure:
STOT RE 2 H373 Calculation method
Aquatic Chronic 1 H410 Calculation method

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.

ZA / EN