SAFETY DATA SHEET

Fosaprepitant Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Fosaprepitant 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
Acute toxicity (Oral) : Category 4
Skin irritation : Category 2
Eye irritation : Category 2A
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Reproductive organs, Prostate)
Long-term (chronic) aquatic hazard : Category 1

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms :

Signal Word : Warning
Hazard Statements :
H302 Harmful if swallowed.
H315 Causes skin irritation.
H319 Causes serious eye irritation.
H373 May cause damage to organs (Reproductive organs, Prostate) 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.
P280 Wear protective gloves/ eye protection/ face protection.

Response:
P314 Get medical advice/ attention if you feel unwell.
P337 + P313 If eye irritation persists: Get medical advice/ attention.
P391 Collect spillage.

Other hazards which do not result in classification:
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosaprepitant</td>
<td>265121-04-8</td>
<td>Acute toxicity (Oral), Category 4 Skin irritation, Category 2 Eye irritation, Category 2A Specific target organ toxicity - repeated exposure (Oral) (Reproductive organs, Prostate), Category 2 Long-term (chronic) aquatic hazard, Category 1</td>
<td>&gt;= 30 -&lt; 50</td>
</tr>
<tr>
<td>Disodium EDTA, dihydrate</td>
<td>6381-92-6</td>
<td>Acute toxicity (Oral), Category 5 Acute toxicity (Inhalation), Category 4 Specific target organ toxicity - repeated exposure (Respiratory Tract), Category 2</td>
<td>&gt;= 1 -&lt; 5</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:
- In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.
- Get medical attention.
- Wash clothing before reuse.
- Thoroughly clean shoes before reuse.

In case of eye contact:
- In case of contact, immediately flush eyes with plenty of water for at least 15 minutes.
- If easy to do, remove contact lens, if worn.
- Get medical attention.

If swallowed:
- If swallowed, DO NOT induce vomiting unless directed to do so by medical personnel.
- Get medical attention.
- Rinse mouth thoroughly with water.
- Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed:
- Harmful if swallowed.
- Causes skin irritation.
- Causes serious eye irritation.
- May cause damage to organs through prolonged or repeated exposure if swallowed.

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
- Nitrogen oxides (NOx)
- Metal oxides

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:
- Use personal protective equipment.
Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

Avoid release to the environment.
Prevent further leakage or spillage if safe to do so.
Retain and dispose of contaminated wash water.
Local authorities should be advised if significant spillages cannot be contained.

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.

Use only with adequate ventilation.

Do not get on skin or clothing.
Do not breathe dust.
Do not swallow.
Do not get in eyes.
Wash skin thoroughly after handling.
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.
Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

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.

Keep in properly labeled containers.
Store in accordance with the particular national regulations.

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>Fosaprepitant</td>
<td>265121-04-8</td>
<td>TWA</td>
<td>200 µg/m³</td>
<td>Internal</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 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**: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance**: powder

**Color**: off-white

**Odor**: odorless

**Odor Threshold**: No data available
SAFETY DATA SHEET

Fosaprepitant Formulation

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
Solubility(ies)
  Water solubility : No data available
Partition coefficient: n-octanol/water
  Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
  Viscosity, dynamic : No data available
  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
Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Fosaprepitant Formulation

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:
Harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 1.435 mg/kg
Method: Calculation method

Acute inhalation toxicity: Acute toxicity estimate: > 10 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Method: Calculation method

Components:
Fosaprepitant:
Acute oral toxicity: LD50 (Rat, female): > 500 mg/kg
LD50 (Mouse, female): > 500 mg/kg

Disodium EDTA, dihydrate:
Acute oral toxicity: LD50 (Rat): 2.800 mg/kg
Remarks: Based on data from similar materials

Acute inhalation toxicity: LC50 (Rat): > 1 mg/l
Exposure time: 6 h
Test atmosphere: dust/mist
Method: OECD Test Guideline 412
Remarks: Based on data from similar materials

Skin corrosion/irritation:
Causes skin irritation.

Components:
Fosaprepitant:
Species: Rabbit
Result: Skin irritation

Disodium EDTA, dihydrate:
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:
Fosaprepitant:
Species: Bovine cornea
Result: Eye irritation

Disodium EDTA, dihydrate:
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Disodium EDTA, dihydrate:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative
Remarks: Based on data from similar materials

Germ cell mutagenicity
Not classified based on available information.

Components:
Fosaprepitant:
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Test system: human lymphoblastoid cells
Result: negative

Test Type: sister chromatid exchange assay
Test system: Chinese hamster ovary cells
Result: negative

Test Type: in vitro test
Test system: rat hepatocytes
Result: negative

Genotoxicity in vivo:
Test Type: In vivo micronucleus test
Species: Mouse
Cell type: Bone marrow
Result: negative

Disodium EDTA, dihydrate:
Genotoxicity in vitro:
Test Type: Chromosome aberration test in vitro
Result: negative
Remarks: Based on data from similar materials

Genotoxicity in vivo:
Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Ingestion
Method: OECD Test Guideline 474
Result: negative
Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:

Fosaprepitant:
Species: Rat, female
Application Route: Oral
Exposure time: 2 Years
Target Organs: Liver
Remarks: Benign tumor(s)
Species: Rat, male and female
Application Route: Oral
Exposure time: 2 Years
Target Organs: Liver, Thyroid
Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

Disodium EDTA, dihydrate:
Species: Rat
Application Route: Ingestion
Exposure time: 103 weeks
Result: negative
Remarks: Based on data from similar materials

Reproductive toxicity
Not classified based on available information.
Components:

Fosaprepitant:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male and female
Fertility: NOAEL: 2.000 mg/kg body weight
Result: negative

Effects on fetal development: Species: Rat, female
General Toxicity Maternal: NOAEL: 2.000 mg/kg body weight
Result: negative

Species: Rabbit, female
General Toxicity Maternal: NOAEL: 25 mg/kg body weight
Result: negative

Disodium EDTA, dihydrate:
Effects on fertility: Test Type: Four-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

STOT-single exposure
Not classified based on available information.

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

Components:

Fosaprepitant:
Routes of exposure: Ingestion
Target Organs: Reproductive organs, Prostate
Assessment: May cause damage to organs through prolonged or repeated exposure.

Disodium EDTA, dihydrate:
Routes of exposure: Inhalation (dust/mist/fume)
Target Organs: Respiratory Tract
Assessment: Shown to produce significant health effects in animals at concentrations of >0.02 to 0.2 mg/l/6h/d.
Repeated dose toxicity

Components:

Fosaprepitant:
Species: Rat, male and female
NOAEL: 2,000 mg/kg
Application Route: Oral
Exposure time: 6 Months
Target Organs: Liver, Thyroid

Species: Dog
LOAEL: 50 mg/kg
Application Route: Oral
Exposure time: 9 Months
Target Organs: Testis

Species: Dog
NOAEL: 32 mg/kg
Application Route: Oral
Exposure time: 1 y
Remarks: No significant adverse effects were reported

Species: Rat
NOAEL: 4 mg/kg
Application Route: Intravenous
Exposure time: 5 Weeks
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: 10 mg/kg
Application Route: Intravenous
Exposure time: 5 Weeks
Remarks: No significant adverse effects were reported

Disodium EDTA, dihydrate:
Species: Rat
NOAEL: 500 mg/kg
Application Route: Ingestion
Exposure time: 13 Weeks
Remarks: Based on data from similar materials

Species: Rat
LOAEL: 0,03 mg/l
Application Route: inhalation (dust/mist/fume)
Exposure time: 4 Weeks
Remarks: Based on data from similar materials

Aspiration toxicity
Not classified based on available information.
Experience with human exposure

Components:

**Fosaprepitant:**

Ingestion: Symptoms: hiccups, Fatigue, liver function change, constipation, Headache, anorexia

### SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

**Fosaprepitant:**

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Pimephales promelas (fathead minnow)): &gt; 0,462 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure time: 96 h</td>
</tr>
<tr>
<td></td>
<td>Method: OECD Test Guideline 203</td>
</tr>
<tr>
<td></td>
<td>Remarks: No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td></td>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

Toxicity to daphnia and other aquatic invertebrates:

<table>
<thead>
<tr>
<th>EC50 (Daphnia magna (Water flea)): &gt; 0,345 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 48 h</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 202</td>
</tr>
<tr>
<td>Remarks: No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

Toxicity to algae/aquatic plants:

<table>
<thead>
<tr>
<th>NOEC (Pseudokirchneriella subcapitata (green algae)): 0,184 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 72 h</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 201</td>
</tr>
<tr>
<td>Remarks: No toxicity at the limit of solubility.</td>
</tr>
<tr>
<td>Based on data from similar materials</td>
</tr>
</tbody>
</table>

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.
Based on data from similar materials

Toxicity to fish (Chronic toxicity):

<table>
<thead>
<tr>
<th>NOEC (Pimephales promelas (fathead minnow)): 0,195 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 32 Days</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 210</td>
</tr>
<tr>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

<table>
<thead>
<tr>
<th>NOEC (Daphnia magna (Water flea)): 0,018 mg/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time: 21 Days</td>
</tr>
<tr>
<td>Method: OECD Test Guideline 211</td>
</tr>
<tr>
<td>Remarks: Based on data from similar materials</td>
</tr>
</tbody>
</table>

M-Factor (Chronic aquatic toxicity):

| 1                                             |

Disodium EDTA, dihydrate:
### Toxicity to fish

Toxicity to fish (LC50, Lepomis macrochirus (Bluegill sunfish)): 159 mg/l  
Exposure time: 96 h
Remarks: Based on data from similar materials

### Toxicity to daphnia and other aquatic invertebrates

Toxicity to daphnia (EC50, Daphnia magna (Water flea)): 140 mg/l  
Exposure time: 48 h
Remarks: Based on data from similar materials

### Toxicity to algae/aquatic plants

Toxicity to algae (EC50, Desmodesmus subspicatus (green algae)): > 100 mg/l  
Exposure time: 72 h
Remarks: Based on data from similar materials

### Toxicity to fish (Chronic toxicity)

Toxicity to fish (NOEC, Danio rerio (zebra fish)): 25,7 mg/l  
Exposure time: 35 d
Method: OECD Test Guideline 210
Remarks: Based on data from similar materials

### Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)

Toxicity to daphnia (NOEC, Daphnia magna (Water flea)): 25 mg/l  
Exposure time: 21 d
Remarks: Based on data from similar materials

### Toxicity to microorganisms

Toxicity to microorganisms (EC50): < 500 mg/l  
Exposure time: 0.5 h
Method: OECD Test Guideline 209
Remarks: Based on data from similar materials

### Persistence and degradability

#### Components:

**Fosaprepitant:**

Biodegradability: Result: not rapidly degradable  
Method: OECD Test Guideline 314

**Disodium EDTA, dihydrate:**

Biodegradability: Result: Inherently biodegradable.  
Biodegradation: 80 - 90 %  
Exposure time: 28 d
Remarks: Based on data from similar materials

### Bioaccumulative potential

#### Components:

**Fosaprepitant:**

Bioaccumulation: Species: Lepomis macrochirus (Bluegill sunfish)  
Bioconcentration factor (BCF): 50,1  
Method: OECD Test Guideline 305
Remarks: Based on data from similar materials
Disodium EDTA, dihydrate:

Bioaccumulation:
- Species: Lepomis macrochirus (Bluegill sunfish)
- Bioconcentration factor (BCF): 1.8
- Remarks: Based on data from similar materials

Partition coefficient: n-octanol/water:
- log Pow: -4.3

Mobility in soil:
No data available

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. (Fosaprepitant)
- Class: 9
- Packing group: III
- Labels: 9

IATA-DGR
- UN/ID No.: UN 3077
- Proper shipping name: Environmentally hazardous substance, solid, n.o.s. (Fosaprepitant)
- 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. (Fosaprepitant)
- Class: 9
- Packing group: III
**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. (Fosaprepitant)
- **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 - (LINACH)**: Not applicable
- **Brazil. List of chemicals controlled by the Federal Police**: 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**

**Full text of other abbreviations**
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.

BR / Z8