1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Fosaprepitant Formulation

Manufacturer or supplier's details
Company : MSD
Address : Briahnager - Off Pune Nagar Road
          Wagholi - Pune - India 412 207
Telephone : +1-908-740-4000
Emergency telephone number : +1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989
Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Acute toxicity (Oral) : Category 4
Skin corrosion/irritation : Category 2
Serious eye damage/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
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.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P273 Avoid release to the environment.
P280 Wear protective gloves/ eye protection/ face protection.

Response:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P319 Get medical help if you feel unwell.
P332 + P317 If skin irritation occurs: Get medical help.
P337 + P317 If eye irritation persists: Get medical help.
P362 + P364 Take off contaminated clothing and wash it before reuse.
P391 Collect spillage.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

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

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosaprepitant</td>
<td>Mixture</td>
</tr>
<tr>
<td>Disodium EDTA, dihydrate</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosaprepitant</td>
<td>265121-04-8</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
<tr>
<td>Disodium EDTA, dihydrate</td>
<td>6381-92-6</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

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

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

In case of skin contact: 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.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media : None known.

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

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 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.

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 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.

**Conditions for safe storage:**
- Keep in properly labelled containers.
- Store in accordance with the particular national regulations.

**Materials to avoid:**
- Do not store with the following product types:
- Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

**Components with workplace control parameters**

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
</table>

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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: Chemical-resistant gloves

Material: Chemical-resistant gloves
Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.

Eye protection: Wear the following personal protective equipment: Safety goggles
Skin and body protection: 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).

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

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Colour: off-white
Odour: odourless
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : May form explosive dust-air mixture during processing, handling or other means.
SAFETY DATA SHEET
Fosaprepitant Formulation

Can react with strong oxidizing agents.

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

Incompatible materials: Oxidizing agents

Hazardous decomposition products: No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity:
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 sensitisation
Skin sensitisation
Not classified based on available information.
Respiratory sensitisation
Not classified based on available information.

Components:
Disodium EDTA, dihydrate:
Test Type: Maximisation Test
Exposure routes: 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 assay
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
: 50 mg/kg body weight
Target Organs : Liver
Remarks : Benign tumor(s)

Species : Rat, male and female
Application Route : Oral
Exposure time : 2 Years
: 250 mg/kg body weight
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 foetal development: Species: Rat, female
General Toxicity Maternal: NOAEL: 2,000 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 foetal development: Test Type: Embryo-foetal 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:

Exposure routes: Ingestion
Target Organs: Reproductive organs, Prostate
Assessment: May cause damage to organs through prolonged or repeated exposure.

Disodium EDTA, dihydrate:

Exposure routes: 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 yr
- **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

12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Fosaprepitant:**

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
Based on data from similar materials

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
Based on data from similar materials

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
Based on data from similar materials

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): NOEC: 0.195 mg/l
Exposure time: 32 Days
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 0.018 mg/l
Exposure time: 21 Days
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211
Remarks: Based on data from similar materials

M-Factor (Chronic aquatic toxicity): 1
Disodium EDTA, dihydrate:

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

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

NOEC (Desmodesmus subspicatus (green algae)): 100 mg/l
Exposure time: 72 h
Remarks: Based on data from similar materials

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

Toxicity to fish (Chronic toxicity): NOEC: 25.7 mg/l
Exposure time: 35 d
Species: Danio rerio (zebra fish)
Method: OECD Test Guideline 210
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 25 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
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

13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (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
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

Transport in bulk according to IMO instruments
Not applicable for product as supplied.

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

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

16. OTHER INFORMATION

Further information

Date format : dd.mm.yyyy

Full text of other abbreviations

AIIC - 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); 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 con-
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.

IN / EN