SAFETY DATA SHEET

Alvimopan Formulation

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

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Alvimopan 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

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

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

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvimopan</td>
<td>170098-38-1</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
Wash with water and soap.
Get medical attention if symptoms occur.
## 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

### 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
- Wear self-contained breathing apparatus for firefighting if necessary.
- Use personal protective equipment.

## SECTION 6. ACCIDENTAL RELEASE MEASURES

### Personal precautions, protective equipment and emergency procedures
- 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.

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. 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>Alvimopan</td>
<td>170098-38-1</td>
<td>TWA</td>
<td>10 µg/m³</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</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
For prolonged or repeated contact use protective gloves. 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
No data available

Odor
No data available

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
Not applicable

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

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

Product:
Acute oral toxicity : Acute toxicity estimate: > 5.000 mg/kg
Method: Calculation method
Acute dermal toxicity : Acute toxicity estimate: > 5.000 mg/kg
Method: Calculation method
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Components:
Alvimopan:
Acute oral toxicity: LD50 (Rat): > 500 mg/kg
LD50 (Mouse): > 4,000 mg/kg
Acute dermal toxicity: LD50 (Mouse): > 2,000 mg/kg
Acute toxicity (other routes of administration): LD50 (Rat): > 20 mg/kg
Application Route: Intravenous
Remarks: No significant adverse effects were reported

Skin corrosion/irritation
Not classified based on available information.

Components:
Alvimopan:
Species: Rabbit
Result: Mild skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:
Alvimopan:
Species: Rabbit
Result: Mild eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Alvimopan:
Test Type: Maximization Test
Routes of exposure: Dermal
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:
Alvimopan:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Test system: mouse lymphoma cells
Result: negative

Genotoxicity in vivo:
Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Mouse
Application Route: Oral
Result: negative

Carcinogenicity
Not classified based on available information.

Components:
Alvimopan:
Species: Rat
Application Route: Oral
Exposure time: 2 Years
NOAEL: 500 mg/kg body weight
Result: negative

Species: Mouse
Application Route: Oral
Exposure time: 2 Years
LOAEL: 4.000 mg/kg body weight
Result: positive
Target Organs: Bone, Skin
Remarks: Benign and malignant tumor(s)
Adverse effects were observed in females only.
These is no evidence that these findings are relevant to hu-
mans.

Reproductive toxicity
Not classified based on available information.

Components:
Alvimopan:
Effects on fertility:
Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Intravenous injection
Fertility: NOAEL: 5 mg/kg body weight
Result: No effects on fertility.

Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Oral
Fertility: NOAEL: 200 mg/kg body weight
Result: No effects on fertility.
Test Type: Fertility/early embryonic development
Species: Rabbit
Application Route: Intravenous
Fertility: NOAEL: 15 mg/kg body weight
Result: No effects on fertility.

Effects on fetal development:
Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 100 mg/kg body weight

Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: 200 mg/kg body weight
Result: Embryo-fetal toxicity.

Test Type: Embryo-fetal development
Species: Rat
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 10 mg/kg body weight
Result: No significant adverse effects were reported

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Intravenous injection
Developmental Toxicity: NOAEL: 15 mg/kg body weight
Result: No significant adverse effects were reported

**STOT-single exposure**
Not classified based on available information.

**STOT-repeated exposure**
Not classified based on available information.

**Repeated dose toxicity**

**Components:**

**Alvimopan:**
Species : Mouse
NOAEL : 1000 mg/kg
Application Route : Oral
Exposure time : 13 Weeks
Remarks : No significant adverse effects were reported

Species : Dog
NOAEL : 1000 mg/kg
Application Route : Oral
Exposure time : 39 Weeks
Remarks : No significant adverse effects were reported

Species : Rat
NOAEL : 500 mg/kg
Application Route: Oral
Exposure time: 1 y
Remarks: No significant adverse effects were reported

Species: Dog
NOAEL: 2 mg/kg
Application Route: Intravenous
Exposure time: 1 Months
Remarks: No significant adverse effects were reported

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:
Alvimopan:
Ingestion: Symptoms: stomach discomfort, Gastrointestinal disturbance, Nausea, Vomiting, Abdominal pain

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
Alvimopan:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 17 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)): > 17 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: No toxicity at the limit of solubility.

Toxicity to algae/aquatic plants: EC50 (Scenedesmus subspicatus): > 17 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: No toxicity at the limit of solubility.

NOEC (Scenedesmus subspicatus): 17 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: No toxicity at the limit of solubility.

Toxicity to microorganisms: EC50: > 920 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 920 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition  
Method: OECD Test Guideline 209

**Persistence and degradability**

**Components:**

**Alvimopan:**  
Biodegradability : Result: Not readily biodegradable.  
Biodegradation: 4%  
Exposure time: 28 d

**Bioaccumulative potential**

**Components:**

**Alvimopan:**  
Partition coefficient: n-octanol/water  
\log \text{Pow}: 0.52

**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**  
Not regulated as a dangerous good

**IATA-DGR**  
Not regulated as a dangerous good

**IMDG-Code**  
Not regulated as a dangerous good

**Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code**  
Not applicable for product as supplied.

**SECTION 15. REGULATORY INFORMATION**

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

Argentina. Carcinogenic Substances and Agents : Not applicable
Registry.

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

International Regulations

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

- 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 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
- SDS - Safety Data Sheet
- TCSI - Taiwan Chemical Substance Inventory
- TDG - Transportation of Dangerous Goods
- TSCA - Toxic Substances Control Act (United States)
- UN - United Na-
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