1. PRODUCT AND COMPANY IDENTIFICATION

Chemical product name : Alvimopan Formulation

Supplier’s company name, address and phone number
Company name of supplier : MSD
Address : Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd.
Menuma factory
Telephone : 048-588-8411
E-mail address : EHSDATASTEWARD@msd.com
Emergency telephone number : +1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS classification of chemical product
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

GHS label elements
Not a hazardous substance or mixture according to the Globally Harmonised System (GHS).

Other hazards which do not result in classification
Important symptoms and outlines of the emergency assumed
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.

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>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvimopan</td>
<td>170098-38-1</td>
<td>&gt;= 1 - &lt; 10</td>
<td></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: 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:
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: No special precautions are necessary for first aid responders.

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

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

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.

7. HANDLING AND STORAGE

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. 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.

Avoidance of contact: Oxidizing agents

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.

Storage

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

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

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

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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical state: powder

Colour: No data available

Odour: No data available

Odour Threshold: No data available

Melting point/freezing point: No data available

Boiling point, initial boiling point and boiling range: No data available

Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids): No data available

Lower explosion limit and upper explosion limit / flammability limit:
- Upper explosion limit / Upper flammability limit: No data available
- Lower explosion limit / Lower flammability limit: No data available
SAFETY DATA SHEET
Alvimopan Formulation

Version: 3.0
Revision Date: 2021/08/27
SDS Number: 643697-00014
Date of last issue: 2020/10/10
Date of first issue: 2016/05/02

Flash point: Not applicable
Decomposition temperature: No data available
pH: No data available
Evaporation rate: No data available
Auto-ignition temperature: No data available
Viscosity
  Viscosity, dynamic: No data available
  Viscosity, kinematic: No data available
Solubility(ies)
  Water solubility: No data available
Partition coefficient: n-octanol/water: No data available
Vapour pressure: No data available
Density and / or relative density
  Density: No data available
  Relative vapour density: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: No data available
Particle characteristics
  Particle size: 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. 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
Not classified based on available information.

Product:
Acute oral toxicity:
- Acute toxicity estimate: > 2,000 mg/kg
  Method: Calculation method

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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.
**Components:**

**Alvimopan:**
- Test Type: Maximisation Test
- Exposure routes: 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.
  - There is no evidence that these findings are relevant to humans.

**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 foetal development:

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

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

Test Type: Embryo-foetal 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-foetal 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:
### Alvimopan Formulation

**Version**: 3.0  
**Revision Date**: 2021/08/27  
**SDS Number**: 643697-00014  
**Date of last issue**: 2020/10/10  
**Date of first issue**: 2016/05/02

<table>
<thead>
<tr>
<th>Species</th>
<th>Mouse</th>
</tr>
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<tbody>
<tr>
<td>NOAEL</td>
<td>1000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>13 Weeks</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>1000 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>39 Weeks</td>
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<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>500 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Oral</td>
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<tr>
<td>Exposure time</td>
<td>1 yr</td>
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<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Intravenous</td>
</tr>
<tr>
<td>Exposure time</td>
<td>1 Months</td>
</tr>
<tr>
<td>Remarks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>

### Aspiration toxicity
Not classified based on available information.

### Experience with human exposure

#### Components:

**Alvimopan**:

- **Ingestion**
  - Symptoms: stomach discomfort, Gastrointestinal disturbance, Nausea, Vomiting, Abdominal pain

### 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
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 Pow: 0.52

Mobility in soil
No data available

Hazardous to the ozone layer
Not applicable

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 : Not applicable
Proper shipping name : Not applicable
Class : Not applicable
Subsidiary risk : Not applicable
Packing group : Not applicable
Labels : Not applicable

IATA-DGR
UN/ID No. : Not applicable
Proper shipping name : Not applicable
Class : Not applicable
Subsidiary risk : Not applicable
Packing group : Not applicable
Labels : Not applicable
Packing instruction (cargo aircraft) : Not applicable
Packing instruction (passenger aircraft) : Not applicable

IMDG-Code
UN number : Not applicable
Proper shipping name : Not applicable
Class : Not applicable
Subsidiary risk : Not applicable
Packing group : Not applicable
Labels : Not applicable
EmS Code : Not applicable
Marine pollutant : Not applicable

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

National Regulations
Refer to section 15 for specific national regulation.

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law
Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.
Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable

Vessel Safety Law
Not regulated as a dangerous good

Aviation Law
Not regulated as a dangerous good
**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>
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</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>2021/08/27</td>
<td>643697-00014</td>
<td>2020/10/10</td>
<td>2016/05/02</td>
</tr>
</tbody>
</table>

### Marine Pollution and Sea Disaster Prevention etc Law

<table>
<thead>
<tr>
<th>Bulk transportation</th>
<th>: Not classified as noxious liquid substance</th>
</tr>
</thead>
</table>

### Marine Pollution and Sea Disaster Prevention etc Law

<table>
<thead>
<tr>
<th>Pack transportation</th>
<th>: Not classified as marine pollutant</th>
</tr>
</thead>
</table>

### Narcotics and Psychotropics Control Act

- Narcotic or Psychotropic Raw Material (Export / Import Permission)
  - Not applicable

- Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
  - Not applicable

### Waste Disposal and Public Cleansing Law

- Industrial waste

#### The components of this product are reported in the following inventories:

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

### 16. OTHER INFORMATION

#### Further information

Sources of key data used to compile the Safety Data Sheet:

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

Date format : yyyy/mm/dd

Full text of other abbreviations

<table>
<thead>
<tr>
<th>AIIC</th>
<th>- Australian Inventory of Industrial Chemicals;</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANTT</td>
<td>- National Agency for Transport by Land of Brazil;</td>
</tr>
<tr>
<td>ASTM</td>
<td>- American Society for the Testing of Materials;</td>
</tr>
<tr>
<td>bw</td>
<td>- Body weight;</td>
</tr>
<tr>
<td>CMR</td>
<td>- Carcinogen, Mutagen or Reproductive Toxicant;</td>
</tr>
<tr>
<td>DIN</td>
<td>- Standard of the German Institute for Standardisation;</td>
</tr>
<tr>
<td>DSL</td>
<td>- Domestic Substances List (Canada);</td>
</tr>
<tr>
<td>ECx</td>
<td>- Concentration associated with x% response;</td>
</tr>
<tr>
<td>ELx</td>
<td>- Loading rate associated with x% response;</td>
</tr>
<tr>
<td>EmS</td>
<td>- Emergency Schedule;</td>
</tr>
<tr>
<td>ENCS</td>
<td>- Existing and New Chemical Substances (Japan);</td>
</tr>
<tr>
<td>ErCx</td>
<td>- Concentration associated with x% growth rate response;</td>
</tr>
<tr>
<td>ERG</td>
<td>- Emergency Response Guide;</td>
</tr>
<tr>
<td>GHS</td>
<td>- Globally Harmonized System;</td>
</tr>
<tr>
<td>GLP</td>
<td>- Good Laboratory Practice;</td>
</tr>
<tr>
<td>IARC</td>
<td>- International Agency for Research on Cancer;</td>
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<tr>
<td>IATA</td>
<td>- International Air Transport Association;</td>
</tr>
<tr>
<td>IBC</td>
<td>- International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk;</td>
</tr>
<tr>
<td>ICAO</td>
<td>- International Civil Aviation Organization;</td>
</tr>
<tr>
<td>IECSC</td>
<td>- Inventory of Existing Chemical Substances in China;</td>
</tr>
<tr>
<td>IMDG</td>
<td>- International Maritime Dangerous Goods;</td>
</tr>
<tr>
<td>IMO</td>
<td>- International Maritime Organization;</td>
</tr>
<tr>
<td>ISHL</td>
<td>- Industrial Safety and Health Law (Japan);</td>
</tr>
<tr>
<td>ISO</td>
<td>- International Organisation for Standardization;</td>
</tr>
<tr>
<td>KECl</td>
<td>- Korea Existing Chemicals Inventory;</td>
</tr>
<tr>
<td>LC50</td>
<td>- Lethal Concentration to 50 % of a test population;</td>
</tr>
<tr>
<td>LD50</td>
<td>- Lethal Dose to 50% of a test population (Median Lethal Dose);</td>
</tr>
<tr>
<td>MARPOL</td>
<td>- International Convention for the Prevention of Pollution from Ships;</td>
</tr>
</tbody>
</table>
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.

 JP / EN