SAFETY DATA SHEET

Alvimopan Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Alvimopan Formulation

Manufacturer or supplier's details
Company name of supplier : MSD
Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
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
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.

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 : Contact with dust can cause mechanical irritation or drying of the skin.
SAFETY DATA SHEET

Alvimopan Formulation

Version 1.11 Revision Date: 10.10.2020 SDS Number: 643699-00012 Date of last issue: 13.09.2019 Date of first issue: 02.05.2016

delayed
Protection of first-aiders: No special precautions are necessary for first aid responders.
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 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 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.

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.

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.

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
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.
- 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
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

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
### 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:

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>NOAEL</th>
<th>Result</th>
<th>Target Organs</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>Oral</td>
<td>2 Years</td>
<td>500 mg/kg body weight</td>
<td>negative</td>
<td>Bone, Skin</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>Oral</td>
<td>2 Years</td>
<td>4,000 mg/kg body weight</td>
<td>positive</td>
<td>Bone, Skin</td>
<td></td>
</tr>
</tbody>
</table>

Adverse effects were observed in females only. These is no evidence that these findings are relevant to humans.

### Reproductive toxicity

Not classified based on available information.

### Components:

#### Alvimopan:

<table>
<thead>
<tr>
<th>Species</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>NOAEL</th>
<th>Result</th>
<th>Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>Intravenous injection</td>
<td>2 Years</td>
<td>5 mg/kg body weight</td>
<td>No effects on fertility.</td>
<td></td>
</tr>
<tr>
<td>Rat</td>
<td>Oral</td>
<td>2 Years</td>
<td>200 mg/kg body weight</td>
<td>No effects on fertility.</td>
<td></td>
</tr>
<tr>
<td>Rabbit</td>
<td>Intravenous</td>
<td></td>
<td>15 mg/kg body weight</td>
<td>No effects on fertility.</td>
<td></td>
</tr>
</tbody>
</table>
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 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.

**Domestic regulation**
- **NOM-002-SCT**
  Not regulated as a dangerous good
- **Special precautions for user**
  Not applicable
SAFETY DATA SHEET

Alvimopan Formulation

SECTION 15. REGULATORY INFORMATION

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

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.

The ingredients of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER 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; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; 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; WHMIS - Workplace Hazardous Materials Information System
SAFETY DATA SHEET

Alvimopan Formulation

Version: 1.11  Revision Date: 10.10.2020  SDS Number: 643699-00012  Date of last issue: 13.09.2019

Date of first issue: 02.05.2016

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

Revision Date: 10.10.2020

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8