SAFETY DATA SHEET
Alvimopan Formulation

SECTION 1. IDENTIFICATION

Product name : Alvimopan Formulation

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Telefax : 908-735-1496
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASETWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust

GHS label elements
Signal Word : Warning
Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

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>Polyethylene glycol</td>
<td>25322-68-3</td>
<td>&gt;= 90 - &lt;= 100</td>
</tr>
<tr>
<td>Alvimopan</td>
<td>170098-38-1</td>
<td>&gt;= 1 - &lt; 5</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

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 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.

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>Polyethylene glycol</td>
<td>25322-68-3</td>
<td>TWA (aerosol)</td>
<td>10 mg/m³</td>
<td>US WEEL</td>
</tr>
<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).
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Date of first issue: 05/02/2016

Personal protective equipment

Respiratory protection: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

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
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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
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.
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:

Polyethylene glycol:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 423
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Remarks: Based on data from similar materials

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:

Polyethylene glycol:
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation
Remarks: Based on data from similar materials

Alvimopan:
Species: Rabbit
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<table>
<thead>
<tr>
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<td>05/02/2016</td>
</tr>
</tbody>
</table>

Result: Mild skin irritation

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

**Components:**

**Polyethylene glycol:**
- **Species:** Rabbit
- **Result:** No eye irritation
- **Method:** OECD Test Guideline 405
- **Remarks:** Based on data from similar materials

**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:**

**Polyethylene glycol:**
- **Test Type:** Maximization Test
- **Routes of exposure:** Skin contact
- **Species:** Guinea pig
- **Result:** negative
- **Remarks:** Based on data from similar materials

**Alvimopan:**
- **Test Type:** Maximization Test
- **Routes of exposure:** Dermal
- **Result:** negative

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Polyethylene glycol:**
- **Genotoxicity in vitro:** Test Type: Bacterial reverse mutation assay (AMES)
  - **Result:** negative
  - **Remarks:** Based on data from similar materials

**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 humans.

IARC  
No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA  
No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP  
No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

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:**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>1000 mg/kg</td>
<td>Oral</td>
<td>13 Weeks</td>
<td>No significant adverse effects were reported</td>
</tr>
</tbody>
</table>
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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:
Polyethylene glycol:
Toxicity to fish: LC50 (Poecilia reticulata (guppy)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Remarks: Based on data from similar materials

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: EC50 (Scenedesmus subspicatus): > 17 mg/l
plants

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:

Polyethylene glycol:
Biodegradability: Result: rapidly degradable
Remarks: Based on data from similar materials

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

Bioaccumulative potential

Components:

Polyethylene glycol:
Partition coefficient: n-octanol/water: log Pow: < 3

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

49 CFR
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards: Combustible dust

SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
Polyethylene glycol 25322-68-3
Alvimopan 170098-38-1

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

AICS: not determined

DSL: not determined

IECSC: not determined
**NFPA 704:**

- **Flammability:** 1
- **Health:** 0
- **Instability:** 0

**HMIS® IV:**

- **HEALTH:** / 0
- **FLAMMABILITY:** 3
- **PHYSICAL HAZARD:** 0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

**Further information**

**Full text of other abbreviations**

- US WEEL: USA. Workplace Environmental Exposure Levels (WEEL)
- US WEEL / TWA: 8-hr TWA

**Abbreviations**

- AICIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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; 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; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concern-
Alvimopan Formulation

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

Revision Date: 10/10/2020

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.

US / Z8