MATERIAL SAFETY DATA SHEET (MSDS)

Section 1. Product and Company Information

<table>
<thead>
<tr>
<th>Substance Name</th>
<th>Enterog® Capsules</th>
<th>MSDS Number</th>
<th>3, Version 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synonyms</td>
<td>Alvimopan formulated product, alvimopan 12 mg capsules, ADL 8-2698, SB-767905-KW, LY246736</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alvimopan Chemical Name</td>
<td>[[2(S)-[[4(R)-(3-hydroxyphenyl)-3(R), 4-dimethyl-l-piperidinyl] methyl]-l-oxo-3-phenylpropyl] amino] acetic acid dihydrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alvimopan Chemical Family</td>
<td>Piperidine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Capsule. Light blue opaque body with light blue opaque cap, hard gelatin capsule imprinted with ADL2698 in black ink on body and cap</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmaceutical Category</td>
<td>Alvimopan is a peripherally acting mu-opioid receptor antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical Indication</td>
<td>Enterog® is indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis.</td>
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<td></td>
</tr>
</tbody>
</table>

Section 2. Composition and Information on Ingredients

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS/EINECS/ELINCS#</th>
<th>Composition (Wt %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvimopan</td>
<td>170098-38-1</td>
<td>3.5 percent</td>
</tr>
<tr>
<td>Non-hazardous</td>
<td>Not Assigned</td>
<td>96.5 percent</td>
</tr>
</tbody>
</table>

Section 3. Hazard Identification

Emergency Overview: Caution – pharmaceutical agent. Overexposure in the workplace may lead to headache and gastrointestinal effects including nausea, vomiting, abdominal pain and soft stools.
Relevant Routes of Exposure      Eyes, Skin, Inhalation, and Ingestion

Signs and Symptoms of Exposure

**Eyes**  May produce slight irritation and stinging.

**Skin**  May produce slight irritation. Stinging may occur if contact occurs with mucous membranes or open wounds. Hypersensitivity reactions may occur.

**Inhalation**  Unknown, effects may be similar to those produced with ingestion (see below). The effects of inhaling the capsule contents, or its vapors, have not been determined. No specific studies have been conducted. Physical form suggests that risk of inhalation is negligible.

**Ingestion**  Ingestion may cause headache, nausea, vomiting, abdominal pain, and soft stools.

Medical Conditions Aggravated By Exposure: Persons with current, prolonged use of opioids, bowel disorders, or hypersensitivity to alvimopan may exhibit greater sensitivity to exposure.

<table>
<thead>
<tr>
<th>Section 4. First Aid Measures - (by medical responders using “Universal Precautions”)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eyes</strong></td>
</tr>
<tr>
<td><strong>Skin</strong></td>
</tr>
<tr>
<td><strong>Inhalation</strong></td>
</tr>
<tr>
<td><strong>Ingestion</strong></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Notes to Health Professionals**  There is no specific antidote. Symptomatic and supportive treatment of adverse effects is recommended. Persons with current, prolonged use of opioids, bowel disorders, or hypersensitivity to alvimopan may exhibit greater sensitivity to exposure.

Refer to Section 11. Toxicological Information, for additional information on toxicity.
Section 5. Fire Fighting Measures

Flashpoint/Test method  Not determined for Entereg® capsules. The flashpoint of alvimopan, the active pharmaceutical ingredient, is > 200 °F (closed cup).

Fire and Explosion Hazards  Not expected for this product, although the packaging is combustible.

Lower Explosive Level/Upper Explosive Level  Not Determined

Extinguishing Media  Water spray, carbon dioxide or dry chemical.

Fire Fighting Instructions  Fight fire from a safe distance. Wear full protective clothing. Use water spray to keep exposed containers and equipment cool. Toxic, corrosive or flammable thermal decomposition products are expected when the product is exposed to fire. Self-contained breathing apparatus and full protective equipment is recommended for firefighters.

Section 6. Accidental Release Measures

Personal Precautions  Personal protective equipment should be worn when cleaning up a spill (See Section 8. Exposure Controls and Personal Protection).

Clean-up Methods  Soak up contents of broken capsules with an absorbent material. Carefully collect material and place in a properly labeled waste container for disposal. Wash area of spill to remove from surfaces. Wash skin thoroughly after handling. No specific decontamination or detoxification procedures have been identified for this product. Take precautions to prevent entry into waterways, sewers, or surface drainage systems.

Section 7. Handling and Storage

Handling  Avoid breaking or crushing capsules.

Storage  No storage requirements are necessary for occupational hazards. Follow product information storage instructions to maintain efficacy.
Work/Hygiene Practices
Handling this product in final form presents minimal risk from occupational exposure. Normal room ventilation is expected to be adequate for routine handling of this product. If capsules are crushed or broken, avoid contact with skin, eyes, and clothing. If contact with skin or clothing occurs, wash affected area thoroughly and change clothing. See also Section 4. First Aid Measures.

Section 8. Exposure Controls and Personal Protection

Preventive Measures
If drug product handling produces broken capsules, a risk assessment of the procedure should be performed.

Engineering Controls
None required for normal handling. If capsules are crushed or broken, active drug substance may be released, and local exhaust ventilation may be required.

Personal Protection:

Eye and Face Protection
Wear approved safety glasses with side shields or goggles where risk of eye exposure exists.

Skin Protection
Avoid skin contact. Impervious gloves should be worn when handling capsules.

Respiratory Protection
None normally required. Respiratory protection should be worn. Respiratory protection must meet compliance with the OSHA 29 CFR 1910.134 and ANSI Z88.2 or equivalent, depending on local regulations.

Exposure Guidelines:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>ACGIH TLV</th>
<th>OSHA PEL</th>
<th>Adolor OEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvimopan drug substance</td>
<td>Not established</td>
<td>Not established</td>
<td>0.4 mg/m³ (8 hour TWA)</td>
</tr>
</tbody>
</table>

Section 9. Physical and Chemical Properties

Appearance/Physical State
Capsule. Light blue opaque body with light blue opaque cap, hard gelatin capsule imprinted with ADL2698 in black ink on body and cap. Alvimopan is contained within a solid matrix.

Melting Point
Not applicable.

Solubility
Not determined for Entereg® capsules. Alvimopan, the active pharmaceutical ingredient in alvimopan capsules, is insoluble in water and soluble in ethanol and dimethyl sulfoxide (DMSO).
Section 10. Stability and Reactivity

Stability
This product is stable under normal handling and storage conditions. Follow product information storage instructions to maintain efficacy.

Conditions to Avoid
Oxidizers, excessive temperatures and an open flame.

Hazardous Decomposition Products
Not determined for Entereg® capsules. Thermal decomposition products of alvimopan, the active pharmaceutical ingredient, include carbon oxides (CO, CO₂), nitrogen oxides (NO, NO₂), sulfur oxides (SOₓ) and smoke.

Hazardous Polymerization
Will not occur.

Section 11. Toxicological Information

Pharmacological Effects
The active pharmaceutical ingredient in this product, alvimopan, is a peripherally acting mu-opioid receptor antagonist.

Oral Toxicity
Not expected to be toxic following ingestion.

Inhalation Toxicity
No studies have been conducted.

Skin Effects
May produce slight irritation. Stinging may occur if contact occurs with mucous membranes or open wounds.

Eye Effects
May produce slight irritation and stinging.

Sensitization
Sensitization to alvimopan (allergic skin reaction) is not expected. Sensitization to other components of the formulation may be possible.

Genetic Toxicity
Not expected to be genotoxic under occupational exposure conditions.

Carcinogenicity
Not expected to produce cancer in humans under occupational exposure conditions. No components are listed as carcinogens by Adolor, IARC, NTP or US OSHA.

Reproductive Effects
Not expected to produce adverse effects on fertility or development under occupational exposure conditions.

Other Adverse Effects
Overexposure in the workplace might have the following effects: headache, nausea, vomiting, abdominal pain, and soft stools.
### Section 12. Ecological Information

**Summary**
This material contains an active pharmaceutical ingredient. Local regulations should be consulted prior to environmental release.

Specific information on alvimopan, the active pharmaceutical ingredient, is provided below.

**Ecotoxicity:**

**Aquatic**

**Activated Sludge**
This material contains an active pharmaceutical ingredient that is not toxic to activated sludge microorganisms.

*IC50:* greater than 1000 mg/L, 3 hours, activated sludge

**Daphnid**
The 48-Hour EC50 for the test material to *Daphnia magna*, based on nominal test concentrations, was 44 mg/L. The No Observed Effect Concentration was 18 mg/L.

*EC50:* 44 mg/L, 48 hours, *Daphnia magna*

**Algal**
This material contains an active pharmaceutical ingredient that was not toxic to algae at saturation in the test.

*EC50:* greater than 18 mg/L, 96 hours, *Scenedesmus subspicatus*, green algae, non-static test

*NOEL:* 18 mg/L, 96 hours, *Scenedesmus subspicatus*, green algae, non-static test

**Fish**
This material contains an active pharmaceutical ingredient that was not toxic to fish at saturation in the test.

*LC50:* greater than 17 mg/L, 96 hours, semi-static test, rainbow trout (*Oncohyncus mykiss*)

*NOEL:* 17 mg/L, 96 hours, semi-static test, rainbow trout (*Oncohyncus mykiss*)
Mobility:

Solubility  This material contains an active pharmaceutical ingredient that, for environmental fate predictions, has limited solubility in water.

Partitioning  This material contains an active pharmaceutical ingredient with octanol/water partition coefficient data that suggests, for environmental fate predictions, the active pharmaceutical ingredient will not have the potential to bioaccumulate in the environment.

Persistence and Degradation:

Hydrolysis  No information available

Biodegradation  No information available

Section 13. Disposal Information

Waste Disposal  Collect for recycling or recovery if possible. The disposal method for rejected products/returned goods must ensure that they cannot be resold or re-used. The recommended method of disposal is incineration.

Regulatory Requirements  Observe all local and national regulations when disposing of this product.

Section 14. Transportation Information

This MSDS should accompany all shipments for reference in the event of spillage or accidental release.

US Department of Transportation (DOT)
Proper Shipping Name  Not regulated in transportation

IATA/ICAO
Proper Shipping Name  Not regulated in transportation

IMDG
Proper Shipping Name  Not regulated in transportation
UN Classification and Labeling

Proper Shipping Name
Transportation and shipping of this material is not restricted. It has no known significant hazard requiring special packaging or labeling for air, maritime, United States or European ground transport purposes.

Section 15. Regulatory Information and Warning Labels

The following regulations apply to storage and/or handling. It is the responsibility of the end user to determine the applicability of these regulations at their specific location.

This product is regulated under the Food, Drug, and Cosmetic Act.

US OSHA 29CFR 1910.1200 This dosage form is exempt from the requirements of the OSHA Hazard Communication Standard

TSCA Status FDA-regulated material is exempt from TSCA

EPCRA Section 313 (SARA Title III) Not listed

EPCRA Section 302 Not listed

CERCLA Not listed

RCRA Not a RCRA hazardous waste.

DOT Not applicable

EU Exempt from requirements of the EU Dangerous Preparations Directive. This product is regulated as a medicinal product, cosmetic product or medical device.

Section 16. Other Key Information

Special Hazards None

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