



Adolor Corporation
700 Pennsylvania Drive
Exton, PA 19341-1127

877-857-7018 (24 h contact)

MATERIAL SAFETY DATA SHEET (MSDS)

Section 1. Product and Company Information

Substance Name	Entereg [®] Capsules	MSDS Number	3, Version 2
Synonyms	Alvimopan formulated product, alvimopan 12 mg capsules, ADL 8-2698, SB-767905-KW, LY246736		
Alvimopan Chemical Name	[[2(S)-[[4(R)-(3-hydroxyphenyl)-3(R), 4-dimethyl-1-piperidinyl] methyl]-1-oxo-3-phenylpropyl] amino] acetic acid dihydrate		
Alvimopan Chemical Family	Piperidine		
Appearance	Capsule. Light blue opaque body with light blue opaque cap, hard gelatin capsule imprinted with ADL2698 in black ink on body and cap		
Pharmaceutical Category	Alvimopan is a peripherally acting mu-opioid receptor antagonist		
Medical Indication	Entereg [®] is indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis.		

Section 2. Composition and Information on Ingredients

Name	CAS/EINECS/ELINCS#	Composition (Wt %)
Alvimopan	170098-38-1	3.5 percent
Non-hazardous ingredients	Not Assigned	96.5 percent

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.

Section 4. First Aid Measures - (by medical responders using "Universal Precautions")

Eyes Exposed eyes should be irrigated with copious amounts of water for at least 15 minutes. If irritation occurs and persists, seek medical attention.

Skin Remove any contaminated clothing. Wash exposed area thoroughly with soap and water. If irritation occurs or persists, seek medical attention.

Inhalation Physical form suggests that risk of inhalation is negligible.

Ingestion Do NOT induce vomiting unless directed to do so by medical personnel.

Never give anything by mouth to an unconscious person. If exposed subject is conscious, give plenty of water to drink. If large quantities of this material are swallowed, call a physician immediately.

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:

Ingredient	ACGIH TLV	OSHA PEL	Adolor OEL
Alvimopan drug substance	Not established	Not established	0.4 mg/m ³ (8 hour TWA)

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, CO ₂), nitrogen oxides (NO, NO ₂), sulfur oxides (SO _x) 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 Respiration 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 (*Oncorhynchus mykiss*)

NOEL: 17 mg/L, 96 hours, semi-static test, rainbow trout (*Oncorhynchus 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

<i>Section 13. Disposal Information</i>	
--	--

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.

<i>Section 14. Transportation Information</i>	
--	--

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
------------------------	------

DISCLAIMER OF EXPRESSED AND IMPLIED WARRANTIES

Although reasonable care has been taken in the preparation of this document, Adolor Corporation extends no warranties and makes no representations as to the accuracy or completeness of the information contained therein, and assumes no responsibility regarding the suitability of this information for the user's intended purposes or for the consequences of its use. Each individual should make a determination as to the suitability of the information for his or her particular purpose(s).