



SAFETY DATA SHEET

Revision Date 29-Sep-2018

Version 2

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

Product identifier

Product Name Linzess

Other means of identification

Product Code FG00094
Synonyms Linaclotide

Recommended use of the chemical and restrictions on use

Recommended Use LINZESS is a guanylate cyclase-C agonist indicated in adults for treatment of:• Irritable bowel syndrome with constipation. (IBS-C) and Chronic idiopathic constipation. (CIC)

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.

Details of the supplier of the safety data sheet

Manufacturer

Allergan plc
5 Giralda Farms
Madison, NJ USA 07940
+1-800-272-5525

E-mail address

SDS@Allergan.com

Emergency telephone number

Emergency Telephone

Call CHEMTREC Day or Night
Within USA or Canada: 1-800-424-9300
Outside USA and Canada: +1-703-741-5970 (collect calls accepted)

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status

This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Acute toxicity - Oral	Category 4
Serious eye damage/eye irritation	Category 2
Specific target organ toxicity (repeated exposure)	Category 2

Label elements

Emergency Overview

Warning

Hazard statements

H302 - Harmful if swallowed
H319 - Causes serious eye irritation
H373 - May cause damage to organs through prolonged or repeated exposure



Appearance Capsule	Physical state Solid	Odor No information available
Chemical Name Linaclotide	Symptoms The most commonly reported adverse reaction is diarrhea.	
Chemical Name Linaclotide	Medical Conditions Aggravated by Exposure This medication is contraindicated in children younger than 6 years old, and avoided in age groups 6-17 years old.	

Precautionary statements

- P270 - Do not eat, drink or smoke when using this product
- P301 + P312 - IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell
- P330 - Rinse mouth
- P264 - Wash face, hands and any exposed skin thoroughly after handling
- P280 - Wear protective gloves/protective clothing/eye protection/face protection
- P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
- P337 + P313 - If eye irritation persists: Get medical advice/attention
- P260 - Do not breathe dust/fume/gas/mist/vapors/spray
- P314 - Get medical advice/attention if you feel unwell
- P501 - Dispose of contents/ container to an approved waste disposal plant

Other Information

Unknown Acute Toxicity 10% of the mixture consists of ingredient(s) of unknown toxicity

Over the counter drugs in their solid form are considered exempt under the criteria of the Federal OSHA Hazard Communication Standard 20 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limit may be surpassed, than can be considered hazardous

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS No.	EINECS	Weight-%
Calcium Chloride	10043-52-4	233-140-8	30 - 60*
MICROCRYSTALLINE CELLULOSE(AVICEL PH102)	9004-34-6	232-674-9	30 - 60*
GELATIN TYPE A NF	9000-70-8	232-554-6	5 - 10*
TALC USP(1656)	14807-96-6	238-877-9	1 - 5*
Linaclotide	851199-59-2	N/A	1 - 5*

*The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST AID MEASURES

First aid measures

General advice	If symptoms persist, call a physician.
Eye contact	Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If symptoms persist, call a physician. Rinse thoroughly with plenty of water for at least 15 minutes, lifting lower and upper eyelids. Consult a physician. Immediately flush with plenty of water. After initial flushing, remove any contact lenses and continue flushing for at least

15 minutes. Keep eye wide open while rinsing.

Skin Contact

Wash off immediately with plenty of water for at least 15 minutes. If skin irritation persists, call a physician. Immediate medical attention is not required. Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.

Inhalation

Remove to fresh air. If symptoms persist, call a physician. Immediate medical attention is not required. Move to fresh air in case of accidental inhalation of vapors.

Ingestion

Immediate medical attention is not required. Rinse mouth. Drink plenty of water. Do NOT induce vomiting. Clean mouth with water and drink afterwards plenty of water. Never give anything by mouth to an unconscious person. Call a physician.

Chemical Name

Linaclotide

Note to physicians

Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Suitable extinguishing media

Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media

None known.

Specific hazards arising from the chemical

Fire may produce irritating, corrosive and/or toxic gases.

Explosion data**Sensitivity to Mechanical Impact**

Not impact sensitive.

Sensitivity to Static Discharge

Fine dust dispersed in air, in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Protective equipment and precautions for firefighters

As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions

Use personal protective equipment as required. Avoid contact with eyes and skin. Evacuate personnel to safe areas. Keep people away from and upwind of spill/leak.

Environmental precautions

Prevent entry into waterways, sewers, basements or confined areas. Do not flush into surface water or sanitary sewer system. Prevent further leakage or spillage if safe to do so. Prevent product from entering drains. See Section 12 for additional ecological information.

Methods for containment

Prevent further leakage or spillage if safe to do so.

Methods for cleaning up

Use personal protective equipment as required. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Take up mechanically, placing in appropriate containers for disposal. Avoid creating dust. Clean contaminated surface thoroughly. Soak up with inert absorbent material. Dam up. Pick up and transfer to properly labeled containers. Sweep up and shovel into suitable containers for disposal. After cleaning, flush away traces with water. Take precautionary measures against static discharges.

7. HANDLING AND STORAGE

Advice on safe handling

Ensure adequate ventilation, especially in confined areas. Use personal protective equipment as required. Use with local exhaust ventilation. Do not breathe dust/fume/gas/mist/vapors/spray.

Storage Conditions

Keep container tightly closed. Keep out of the reach of children. Keep containers tightly closed in a cool, well-ventilated place. Keep in properly labeled containers.

Incompatible materials None known based on information supplied.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines

Chemical Name	ACGIH TLV	OSHA PEL	NIOSH IDLH	Allergan OEL (ug/m ³)
MICROCRYSTALLINE CELLULO(AVICEL PH102) 9004-34-6	TWA: 10 mg/m ³	TWA: 15 mg/m ³ total dust TWA: 5 mg/m ³ respirable fraction (vacated) TWA: 15 mg/m ³ total dust (vacated) TWA: 5 mg/m ³ respirable fraction (vacated) TWA: 5 mg/m ³ (vacated) STEL: 10 mg/m ³	TWA: 10 mg/m ³ total dust TWA: 5 mg/m ³ respirable dust TWA: 1 mg/m ³	N/A
TALC USP(1656) 14807-96-6	TWA: 2 mg/m ³ particulate matter containing no asbestos and <1% crystalline silica, respirable particulate matter	(vacated) TWA: 2 mg/m ³ respirable dust <1% Crystalline silica, containing no Asbestos TWA: 20 mppcf if 1% Quartz or more;use Quartz limit	IDLH: 1000 mg/m ³ TWA: 2 mg/m ³ containing no Asbestos and <1% Quartz respirable dust	N/A
Linacotide 851199-59-2	N/A	N/A	N/A	30

NIOSH IDLH *Immediately Dangerous to Life or Health*

Other Information Vacated limits revoked by the Court of Appeals decision in AFL-CIO v. OSHA, 965 F.2d 962 (11th Cir., 1992).

Appropriate engineering controls

Engineering Controls The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/face protection No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, safety glasses should be considered.

Skin and body protection During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. Use appropriate protective clothing for the task (e.g., lab coat, etc.).

Respiratory protection Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	Solid	Appearance	Capsule
Color	No information available	Odor	No information available
Odor threshold	No information available		

<u>Property</u>	<u>Values</u>
pH	No information available
Melting point/freezing point	No information available
Boiling point / boiling range	No information available
Flash point	No information available
Evaporation rate	No information available
Flammability (solid, gas)	No information available
Flammability Limit in Air	
Upper flammability limit:	No information available
Lower flammability limit:	No information available
Vapor pressure	No information available
Vapor density	No information available
Specific Gravity	No information available
Water solubility	No information available
Solubility in other solvents	No information available
Partition coefficient	No information available
Autoignition temperature	No information available
Decomposition temperature	No information available
Explosive properties	No information available
Oxidizing properties	No information available

Other Information

Molecular weight	No information available
VOC Content (%)	No information available
Density	No information available
Bulk density	No information available

10. STABILITY AND REACTIVITY

Reactivity

Not defined As Reactive substance

Chemical stability

Stable under normal conditions.

Possibility of Hazardous Reactions

None under normal processing.

Conditions to avoid

Aerosol formation.

Incompatible materials

None known based on information supplied.

Hazardous Decomposition Products

None known based on information supplied.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure**Acute toxicity**

Chemical Name	Inhalation	Eye contact	Skin Contact	Ingestion
Linaclotide	See Symptoms for more information.	See Symptoms for more information.	Linaclotide was not irritating to rabbit skin and was minimally irritating (reversibly) to rabbit eyes.	See Symptoms for more information.

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
Calcium Chloride	= 1000 mg/kg (Rat)	> 5000 mg/kg (Rabbit)	N/A
MICROCRYSTALLINE CELLULOSE(AVICEL PH102)	> 5 g/kg (Rat)	> 2 g/kg (Rabbit)	> 5800 mg/m ³ (Rat) 4 h

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Chemical Name	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Effects on or via lactation
Linaclotide	Not genotoxic in the in vitro chromosomal aberration assay in cultured human peripheral blood lymphocytes.	In 2-year carcinogenicity studies, linaclotide was not tumorigenic in rats at doses up to 3500 mcg/kg/day or in mice at doses up to 6000 mcg/kg/day. The maximum recommended human dose is approximately 5 mcg/kg/day based on a 60-kg bodyweight.	Linaclotide had no effect on fertility or reproductive function in male and female rats at oral doses of up to 100,000 mcg/kg/day.	It is not known whether the drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this drug is administered to nursing mothers.

Chemical Name	STOT - single exposure	STOT - repeated exposure
Linaclotide	No information available.	In a 13-week rat study, no evidence of toxicity was seen at up to 100 mg/kg/day (the highest dose tested). In a 26-week mouse study, early mortality resulting in dose reduction was seen at the highest dose tested, (100/80 mg/kg/day), but no other signs of target organ toxicity or clinical pathology were seen. A NOAEL of 20 mg/kg/day was identified in this study. In a 39-week monkey study, a NOAEL of 5 mg/kg/day was identified based on an increased incidence of watery stools. No other signs of toxicity were reported; effects were reversible after cessation of treatment. A summary of these data are : Type Route Species Dose MTD Oral Rat >100 mg/kg/day (13-week study) MTD Oral Monkey >50 mg/kg/day (13-week study) MTD Oral Mouse 20 mg/kg/day (26-week study).

Chronic toxicity Avoid repeated exposure.
Target Organ Effects Central Vascular System (CVS), Eyes, Gastrointestinal tract (GI), Respiratory system, Skin.

Numerical measures of toxicity - Product Information

Unknown Acute Toxicity 10% of the mixture consists of ingredient(s) of unknown toxicity
The following values are calculated based on chapter 3.1 of the GHS document .
ATEmix (oral) 1724 mg/kg
ATEmix (dermal) 2565 mg/kg
ATEmix (inhalation-dust/mist) 14.5 mg/l

12. ECOLOGICAL INFORMATION

Ecotoxicity

48% of the mixture consists of component(s) of unknown hazards to the aquatic environment

Chemical Name	Algae/aquatic plants	Fish	Crustacea
Calcium Chloride 10043-52-4	N/A	10650: 96 h Lepomis macrochirus mg/L LC50 static	2280000 - 3948000: 48 h Daphnia magna µg/L LC50
TALC USP(1656) 14807-96-6	N/A	100: 96 h Brachydanio rerio g/L LC50 semi-static	N/A

Chemical Name	Persistence and degradability	Bioaccumulation	Mobility	Partition coefficient
Linaclotide 851199-59-2	N/A	N/A	N/A	0.663

Other adverse effects No information available

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated packaging Do not reuse container. Dispose of contents/containers in accordance with local regulations.

14. TRANSPORT INFORMATION

DOT Not regulated
TDG Not regulated
ICAO (air) Not regulated
IATA Not regulated
IMDG Not regulated
ADR Not regulated
ADN Not regulated

15. REGULATORY INFORMATION

International Inventories

TSCA Not Listed
DSL/NDSL Not Listed
EINECS/ELINCS Not Listed

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances

US Federal Regulations

Carcinogenicity The table below indicates whether each agency has listed any ingredient as a carcinogen. This product contains one or more substances which are classified by IARC as carcinogenic to humans (Group I), probably carcinogenic to humans (Group 2A) or possibly carcinogenic to humans (Group 2B).

Chemical Name	ACGIH	IARC	NTP	OSHA
MICROCRYSTALLINE CELLULOSE(AVICEL PH102) 9004-34-6	-	Group 1	Known	X
TALC USP(1656) 14807-96-6	-	Group 3	-	X

*IARC (International Agency for Research on Cancer)
 Not classifiable as a human carcinogen*

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

Acute health hazard Yes
Chronic Health Hazard No
Fire hazard No
Sudden release of pressure hazard No
Reactive Hazard No

CWA (Clean Water Act)

This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA

This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material

US State Regulations

California Proposition 65

This product does not contain any Proposition 65 chemicals

U.S. State Right-to-Know Regulations

Chemical Name	New Jersey	Massachusetts	Pennsylvania
MICROCRYSTALLINE CELLULOSE(AVICEL PH102) 9004-34-6	X	X	X
Titanium Dioxide 1317-70-0	-	-	X
TALC USP(1656) 14807-96-6	X	X	X

16. OTHER INFORMATION

Revision Date 29-Sep-2018
 Revision Note No information available

Disclaimer

The information provided in this Material Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

End of Safety Data Sheet