PADCEV™ (enfortumab vedotin-ejfv) for Injection

Safety Data Sheet

According To Federal Register / Vol. 77, No. 58 / Monday, March 26, 2012 / Rules And Regulations And According To The Hazardous Products Regulation (February 11, 2015).

Date of Issue: 04/14/2023 Version: 1.0

SECTION 1: IDENTIFICATION

1.1. Product Identifier

Product Form: Mixture

Product Name: PADCEV™ (enfortumab vedotin-ejfv) for Injection

Chemical Name: Proprietary

Formula: Proprietary

Synonyms: ASP7465, AS2567465-00, ASG-22CE

1.2. Intended Use of the Product

Pharmaceutical research, manufacturing and clinical use. For professional use only. For R&D use only.

1.3. Name, Address, and Telephone of the Responsible Party

Company

Astellas US LLC
2375 Waterview Drive
Northbrook, IL 60062
Tel.: 800-888-7704
www.us.astellas.com

1.4. Emergency Telephone Number

Emergency Number : 800-727-7003
Medical Communications

SECTION 2: HAZARDS IDENTIFICATION

2.1. Classification of the Substance or Mixture

GHS-US/CA Classification

Repr. 2	H361
STOT RE 1	H372
Comb. Dust	

Full text of hazard classes and H-statements : see section 16

2.2. Label Elements

GHS-US/CA Labeling

Hazard Pictograms (GHS-US/CA) :

GHS08

Signal Word (GHS-US/CA) : Danger

Hazard Statements (GHS-US/CA) : May form combustible dust concentrations in air.
H361 - Suspected of damaging fertility or the unborn child.
H372 - Causes damage to organs through prolonged or repeated exposure.

Precautionary Statements (GHS-US/CA) : P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P260 - Do not breathe dust.
P264 - Wash hands, forearms, and other exposed areas thoroughly after handling.
P270 - Do not eat, drink or smoke when using this product.
P280 - Wear protective gloves, protective clothing, and eye protection.
P308+P313 - If exposed or concerned: Get medical advice/attention.
P314 - Get medical advice/attention if you feel unwell.
P405 - Store locked up.
P501 - Dispose of contents/container in accordance with local, regional, national, and international regulations.

Supplemental Information : Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. Proper grounding procedures to avoid static electricity should be followed. Prevent dust accumulation (to minimize explosion hazard). Avoid generating dust.

2.3. Other Hazards

The toxicological properties of this substance have not been fully investigated. Exposure may aggravate pre-existing eye, skin, or respiratory conditions.

2.4. Unknown Acute Toxicity (GHS-US/CA)

14.5% of the mixture consists of ingredient(s) of unknown acute toxicity (Oral)

14.5% of the mixture consists of ingredient(s) of unknown acute toxicity (Dermal)

14.5% of the mixture consists of ingredient(s) of unknown acute toxicity (Inhalation (Dust/Mist))

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substance

Not applicable

3.2. Mixture

Name	Synonyms	Product Identifier	% *	GHS Ingredient Classification
Trehalose dihydrate	.alpha.-D-Glucopyranoside, .alpha.-D-glucopyranosyl, dihydrate / .alpha.-D-Glucopyranosyl .alpha.-D-glucopyranoside dihydrate / Trehalose, dihydrate / D-(+)-Trehalose dihydrate	(CAS-No.) 6138-23-4	79.8	Comb. Dust
Enfortumab vedotin		(CAS-No.) 1346452-25-2	14.5	Repr. 2, H361 STOT RE 1, H372
Histidine, L-, monohydrochloride monohydrate	L-Histidine, monohydrochloride, monohydrate / Histidine, monohydrochloride, monohydrate, L- / Histidine-L hydrochloride monohydrate / L-Histidine monohydrochloride monohydrate / (2S)-2-Amino-3-(1H-imidazol-4-yl) propanoic acid hydrate hydrochloride	(CAS-No.) 5934-29-2	3.4	Comb. Dust
L-Histidine	Glyoxaline-5-alanine / Histidine / Histidine, L- / HISTIDINE / L-(-) Histidine / l-Histidine	(CAS-No.) 71-00-1	2	Comb. Dust
Polyoxyethylene sorbitan monolaurate	Polysorbate 20 / Sorbitan monolaurate, ethoxylated / Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivatives / Polyoxyethylene (20) sorbitan monolaurate / PEG-10 SORBITAN LAURATE / PEG sorbitan laurate / Ethoxylated sorbitan monolaurate / Polyethylene glycol sorbitan monolaurate / PEG-40 sorbitan laurate / PEG-75 sorbitan laurate / PEG-44 sorbitan laurate / PEG-80 sorbitan laurate / Polysorbate 21 / PEG-10 sorbitan laurate / Sorbitan monolaurate, ethoxylate / Bioactivator NN-21	(CAS-No.) 9005-64-5	0.3	Not classified

Full text of H-phrases: see section 16

*Percentages are listed in weight by weight percentage (w/w%) for liquid and solid ingredients. Gas ingredients are listed in volume by volume percentage (v/v%).

SECTION 4: FIRST AID MEASURES

4.1. Description of First-aid Measures

General: Never give anything by mouth to an unconscious person. If you feel unwell, seek medical advice (show the label where possible).

Inhalation: Using proper respiratory protection, move the exposed person to fresh air at once. Encourage exposed person to cough, spit out, and blow nose to remove dust. Immediately call a poison center, physician, or emergency medical service.

Skin Contact: Remove contaminated clothing. Drench affected area with water for at least 15 minutes. Obtain medical attention if irritation develops or persists.

Eye Contact: Rinse cautiously with water for at least 15 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention.

Ingestion: Rinse mouth. Do NOT induce vomiting. Obtain medical attention.

4.2. Most Important Symptoms and Effects Both Acute and Delayed

General: Pharmaceutical. When handling in workplace settings, in quantities that are most likely above the therapeutic dose, this product may be harmful if absorbed through the eyes, skin, or respiratory tract.

Inhalation: Dust may be harmful or cause irritation.

Skin Contact: Prolonged exposure may cause skin irritation.

Eye Contact: May cause slight irritation to eyes.

Ingestion: Ingestion may cause adverse effects.

Chronic Symptoms: Suspected of damaging fertility or the unborn child. Causes damage to organs through prolonged or repeated exposure.

4.3. Indication of Any Immediate Medical Attention and Special Treatment Needed

If exposed or concerned, get medical advice and attention. If medical advice is needed, have product container or label at hand.

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Use extinguishing media appropriate for surrounding fire.

Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

5.2. Special Hazards Arising From the Substance or Mixture

Fire Hazard: Combustible Dust.

Explosion Hazard: Dust explosion hazard in air.

Reactivity: Hazardous reactions will not occur under normal conditions.

5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire.

Firefighting Instructions: Use water spray or fog for cooling exposed containers.

Protection During Firefighting: Do not enter fire area without proper protective equipment, including respiratory protection.

Hazardous Combustion Products: Carbon oxides (CO, CO_2). Nitrogen oxides.

Other Information: Risk of dust explosion.

5.4. Reference to Other Sections

Refer to Section 9 for flammability properties.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Do not get in eyes, on skin, or on clothing. Do not breathe dust. Avoid generating dust. Remove ignition sources. Keep away from heat, hot surfaces, sparks, open flames, and other ignition sources. No smoking.

6.1.1. For Non-Emergency Personnel

Protective Equipment: Use appropriate personal protective equipment (PPE).

Emergency Procedures: Evacuate unnecessary personnel.

6.1.2. For Emergency Personnel

Protective Equipment: Equip cleanup crew with proper protection.

Emergency Procedures: Upon arrival at the scene, a first responder is expected to recognize the presence of dangerous goods, protect oneself and the public, secure the area, and call for the assistance of trained personnel as soon as conditions permit. Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters.

6.3. Methods and Materials for Containment and Cleaning Up

For Containment: Contain solid spills with appropriate barriers and prevent migration and entry into sewers or streams. Avoid generation of dust during clean-up of spills.

Methods for Cleaning Up: Clean up spills immediately and dispose of waste safely. Contact competent authorities after a spill. Use explosion proof vacuum during cleanup, with appropriate filter. Do not mix with other materials. Vacuum clean-up is preferred. If sweeping is required use a dust suppressant. Use only non-sparking tools.

6.4. Reference to Other Sections

See Section 8 for exposure controls and personal protection and Section 13 for disposal considerations.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Additional Hazards When Processed: Accumulation and dispersion of dust with an ignition source can cause a combustible dust explosion. Keep dust levels to a minimum and follow applicable regulations.

Precautions for Safe Handling: Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work. Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not get in eyes, on skin, or on clothing. Do not breathe dust. Avoid creating or spreading dust. Keep away from heat, sparks, open flames, hot surfaces. – No smoking.

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations. Avoid creating or spreading dust. Use explosion-proof electrical, ventilating, lighting equipment. Proper grounding procedures to avoid static electricity should be followed.

Storage Conditions: Keep container closed when not in use. Store in a dry, cool place. Keep/Store away from direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Materials: Strong oxidizers.

7.3. Specific End Use(s)

Pharmaceutical research, manufacturing and clinical use. For professional use only. For R&D use only.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameters

For substances listed in section 3 that are not listed here, there are no established Exposure limits from the manufacturer, supplier, importer, or the appropriate advisory agency including: ACGIH (TLV), AIHA (WEEL), NIOSH (REL), OSHA (PEL), or Canadian provincial governments.

8.2. Exposure Controls

Appropriate Engineering Controls: Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Ensure adequate ventilation, especially in confined areas. Ensure all national/local regulations are observed. Proper grounding procedures to avoid static electricity should be followed. Use explosion-proof equipment. Use local exhaust or general dilution ventilation or other suppression methods to maintain dust levels below exposure limits. Power equipment should be equipped with proper dust collection devices. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment.

Personal Protective Equipment: Gloves. Protective clothing. Protective goggles. Insufficient ventilation: wear respiratory protection.

Materials for Protective Clothing: Chemically resistant materials and fabrics.

Hand Protection: Wear protective gloves.

Eye and Face Protection: Chemical safety goggles.

Skin and Body Protection: Wear suitable protective clothing.

Respiratory Protection: If exposure limits are exceeded or irritation is experienced, approved respiratory protection should be worn. In case of inadequate ventilation, oxygen deficient atmosphere, or where exposure levels are not known wear approved respiratory protection.

Other Information: When using, do not eat, drink or smoke.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State	:	Solid
Appearance	:	White to off-white
Odor	:	Not available
Odor Threshold	:	Not available
pH	:	Not available
Evaporation Rate	:	Not available
Melting Point	:	Not available
Freezing Point	:	Not available
Boiling Point	:	Not available
Flash Point	:	Not available
Auto-ignition Temperature	:	Not available
Decomposition Temperature	:	Not available
Flammability (solid, gas)	:	Not available
Lower Flammable Limit	:	Not available
Upper Flammable Limit	:	Not available
Vapor Pressure	:	Not available
Relative Vapor Density at 20°C	:	Not available
Relative Density	:	Not available
Specific Gravity	:	Not available
Solubility	:	Not available
Partition Coefficient: N-Octanol/Water	:	Not available
Viscosity	:	Not available

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity: Hazardous reactions will not occur under normal conditions.

10.2. Chemical Stability: Stable under recommended handling and storage conditions (see section 7).

10.3. Possibility of Hazardous Reactions: Hazardous polymerization will not occur.

10.4. Conditions to Avoid: Direct sunlight, extremely high or low temperatures, and incompatible materials. Sparks, heat, open flame and other sources of ignition. Dust accumulation (to minimize explosion hazard).

10.5. Incompatible Materials: Strong oxidizers.

10.6. Hazardous Decomposition Products: Thermal decomposition generates: Carbon oxides (CO, CO_2). Nitrogen oxides.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on Toxicological Effects - Product

Acute Toxicity (Oral): Not classified

Acute Toxicity (Dermal): Not classified

Acute Toxicity (Inhalation): Not classified

LD50 and LC50 Data: Not available

Enfortumab vedotin for Injection	
Additional information	ADI=120 µg/day

Skin Corrosion/Irritation: Not classified

Enfortumab vedotin for Injection	
Additional information	Injection site microscopic findings consisted of increased mitotic figures and single cell necrosis in the epidermis and/or adnexa including hair follicles and sebaceous glands, epidermal

	acanthosis, perivascular mononuclear infiltrates, and fibrosis. These minimal to mild findings were considered related to antigen expression in the skin and the pharmacology of MMAE, and were generally reversible.

Eye Damage/Irritation: Not classified

Respiratory or Skin Sensitization: Not classified

Germ Cell Mutagenicity: Not classified

Enfortumab vedotin for Injection	
Additional information	Genotoxicity studies were performed on the cytotoxic agent, MMAE. MMAE was aneugenic in the in vivo rat bone marrow micronucleus study, consistent with the pharmacological effect of MMAE on the mitotic apparatus (disruption of the microtubular network). MMAE had no discernible in vitro genotoxic potential in a reverse mutation test in bacteria (Ames test) or in a L5178Y thymidine kinase (TK)+/- mouse lymphoma mutation assay. Monomethyl auristatin E (MMAE) is the cytotoxic component of this antibody drug conjugate. MMAE is an antineoplastic agent that blocks microtubule polymerization and inhibits cell division. Maleimide which is a component of linker showed mutagenicity in Ames test and mouse lymphoma assay.

Carcinogenicity: Not classified

Specific Target Organ Toxicity (Repeated Exposure): Causes damage to organs through prolonged or repeated exposure.

Enfortumab vedotin for Injection	
Additional information	13-week toxicity study in rats no recovery period: (0.5, 2.0, and 5.0 mg/kg/week, i.v. injection once every week for a total of 12 doses). Maximum Tolerated Dose: 5 mg/kg At 0.5 mg/kg/week and above target organ of toxicity included eye, skin/injection site and altered erythrocytic parameters. At 5 mg/kg/week target organ toxicities and secondary changes included; the liver, the testes, and epididymis. 4-week toxicity study in rats with a 6-week recovery period: (0, 2, 5, 10 mg/kg/week, iv injection, once every week for a total of 4 doses). NOAEL: < 2 mg/kg At 2 mg/kg/week and above target organs of toxicity and secondary changes included the testes and epididymis. At 5 mg/kg/week and above target organs of toxicity and secondary changes included the liver, skin, bone marrow, and altered erythrocytic parameters. All findings except testicular findings were reversible by the end of the 4-week recovery period. 4-week toxicity study in cynomolgus monkeys with a 6-week recovery period: (0, 1, 3, 6 mg/kg/week, iv infusion, once every week for a total of 4 doses) NOAEL: 3 mg/kg At 1 mg/kg/week and above target organs of toxicity were the injection site and skin. At 3 mg/kg/week and above altered erythrocytic parameters were noted. At 6 mg/kg lethargy and mortality was observed.

Reproductive Toxicity: Suspected of damaging fertility or the unborn child.

Enfortumab vedotin for Injection	
Additional information	Enfortumab vedotin showed embryo-fetal toxicities. Pregnant rats intravenously administered enfortumab vedotin on GD 6 and 13 at 2 and 5 mg/kg resulted in increases in post implantation loss and decreases in the number of viable fetuses. The surviving fetuses had an increased incidence of skeletal variations.

Specific Target Organ Toxicity (Single Exposure): Not classified

Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: Dust may be harmful or cause irritation.

Symptoms/Injuries After Skin Contact: Prolonged exposure may cause skin irritation.

Symptoms/Injuries After Eye Contact: May cause slight irritation to eyes.

Symptoms/Injuries After Ingestion: Ingestion may cause adverse effects.

Chronic Symptoms: Suspected of damaging fertility or the unborn child. Causes damage to organs through prolonged or repeated exposure.

11.2. Information on Toxicological Effects - Ingredient(s)

LD50 and LC50 Data:

L-Histidine (71-00-1)	
LD50 Oral Rat	> 15 g/kg

Polyoxyethylene sorbitan monolaurate (9005-64-5)	
LD50 Oral Rat	> 18000 mg/kg

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

Ecology - General: Not classified.

12.2. Persistence and Degradability

Enfortumab vedotin for Injection	
Persistence and Degradability	Not established.

12.3. Bioaccumulative Potential

Enfortumab vedotin for Injection	
Bioaccumulative Potential	Not established.

12.4. Mobility in Soil

Not available

12.5. Other Adverse Effects

Other Information: Avoid release to the environment.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Waste Disposal Recommendations: Dispose of contents/container in accordance with local, regional, national, and international regulations

Additional Information: Container may remain hazardous when empty. Continue to observe all precautions.

Ecology - Waste Materials: Avoid release to the environment.

SECTION 14: TRANSPORT INFORMATION

The shipping description(s) stated herein were prepared in accordance with certain assumptions at the time the SDS was authored, and can vary based on a number of variables that may or may not have been known at the time the SDS was issued.

14.1. In Accordance with DOT Not regulated for transport

14.2. In Accordance with IMDG Not regulated for transport

14.3. In Accordance with IATA Not regulated for transport

14.4. In Accordance with TDG Not regulated for transport

SECTION 15: REGULATORY INFORMATION

15.1. US Federal Regulations

Enfortumab vedotin for Injection	
SARA Section 311/312 Hazard Classes	Physical hazard - Combustible dust Health hazard - Reproductive toxicity Health hazard - Specific target organ toxicity (single or repeated exposure)

L-Histidine (71-00-1)
Listed on the United States TSCA (Toxic Substances Control Act) inventory

Polyoxyethylene sorbitan monolaurate (9005-64-5)	
Listed on the United States TSCA (Toxic Substances Control Act) inventory	
EPA TSCA Regulatory Flag	XU - XU - indicates a substance exempt from reporting under the Chemical Data Reporting Rule, (40 CFR 711).

15.2. US State Regulations

Neither this product nor its chemical components appear on any US state lists, or its chemical components are not required to be disclosed.

15.3. Canadian Regulations

L-Histidine (71-00-1)
Listed on the Canadian DSL (Domestic Substances List)

Polyoxyethylene sorbitan monolaurate (9005-64-5)
Listed on the Canadian DSL (Domestic Substances List)

SECTION 16: OTHER INFORMATION, INCLUDING DATE OF PREPARATION OR LAST REVISION

Date of Preparation or Latest Revision : 06/19/2019

Other Information : This document has been prepared in accordance with the SDS requirements of the OSHA Hazard Communication Standard 29 CFR 1910.1200 and Canada's Hazardous Products Regulations (HPR) SOR/2015-17.

GHS Full Text Phrases:

Comb. Dust	Combustible Dust
Repr. 2	Reproductive toxicity Category 2
STOT RE 1	Specific target organ toxicity (repeated exposure) Category 1
H361	Suspected of damaging fertility or the unborn child
H372	Causes damage to organs through prolonged or repeated exposure

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.

NA GHS SDS 2015 (Can, US)