Kyprolis™ (Carfilzomib) Safety Data Sheet

Revision Number: 3 **Date Issued** 09-Sep-2015

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERSTANDING

1.1 Product identifier

Product Name: Kyprolis™ (Carfilzomib)
Common Name: Carfilzomib
Chemical Name: (2S)-N-((S)-1-((S)-4-methyl-1-((R)-2-methyloxiran-2-yl)-1-oxopentan-2-ylcarbamoyl)-2-phenylethyl)-2-((S)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-4-methylpentanamide
Synonyms: No information available

1.2 Relevant identified uses of the substance or mixture and uses advised against

Recommended Use: Pharmaceutical
Uses advised against: No information available

Manufacturer:

Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799
1-805-447-7233
1-805-447-1000

Emergency Telephone Number:

Chemtrec
NORTH AMERICA 1-800-424-9300,
INTERNATIONAL 1-703-527-3887

2. HAZARDS IDENTIFICATION

Emergency Overview

Pharmaceutical product intended for clinical and manufacturing purposes only. Product contains carfilzomib, an active pharmaceutical ingredient, for treatment of multiple myeloma. Dosage contents may pose a health hazard only if significant absorption occurs (e.g. inhalation after a major spill). Avoid inhalation, skin contact, eye contact, and accidental ingestions. Based on available data, the GHS classification criteria are not met.

2.1 - Classification of the drug substance or mixture (drug product in final form, not applicable)

REGULATION (EC) No 1272/2008

Based on available data, the GHS classification criteria are not met.

Classification according to EU Directives 67/548/EEC or 1999/45/EC
For the full text of the R phrases mentioned in this Section, see Section 16

2.2 Label elements

Based on available data, the GHS classification criteria are not met.

2.3 Other Hazards No information available

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Ingredients:	See below
Chemical Name:	(2S)-N-((S)-1-((S)-4-methyl-1-((R)-2-methyloxiran-2-yl)-1-oxopentan-2-ylcarbamoyl)-2-phenylethyl)-2-((S)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-4-methylpentanamide
CAS-No:	868540-17-4

4. FIRST AID MEASURES

4.1 Description of first-aid measures

Eye Contact:	In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Skin Contact:	Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. Consult a physician if necessary.
Inhalation:	Move to fresh air. If symptoms persist, call a physician.
Ingestion:	If symptoms persist, call a physician. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.
Notes to Physician:	Treat symptomatically.

5. FIRE-FIGHTING MEASURES

5.1 Extinguishing media

Flammable Properties: No information available.

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

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No information available.

5.3 Advice for firefighters

Protective Equipment and Precautions for Firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, NIOSH (approved) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

Spill Procedures: If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment in cleaning up a spill. If in powder form, wet down spilled material to minimize airborne dispersion. Soak up material with absorbent e.g., paper towels, and wash spill area thoroughly with appropriate cleaning materials. Dispose of collected material in accordance with applicable waste disposal regulations. Avoid release to the environment.

7. HANDLING AND STORAGE

7.1 Precautions for Safe Handling

Handling and Storage: Avoid contact with skin, eyes or clothing. Do not eat, drink or smoke in work areas. Use adequate ventilation to minimize exposure. Wash hands, face and other potentially exposed areas immediately after handling this material. Remove contaminated clothing prior to entering eating areas. Clean protective equipment thoroughly after each use. Store in a well ventilated area.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control parameters

Occupational Exposure Limit: No exposure guidelines established by ACGIH, NIOSH or OSHA. Amgen recommends an occupational exposure limit (OEL) of 6 µg/m^3 as an 8-hour time weighted average over a 40-hour work week. The OEL is designed as an acceptable airborne concentration of a substance for which it is believed that workers may be repeatedly exposed day after day without adverse health effects. Carfilzomib has been classified per Amgen's Hazard Classification System as an Occupational Exposure Band 4 compound (5 µg/m^3 - 20 µg/m^3).

Engineering Controls: When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.

8.2 Exposure controls

Personal Protective Equipment

Eye/face Protection: Wear safety glasses with side shields, chemical splash goggles, or safety glasses with side shields and a full-face shield to prevent contact with eyes. The choice of protection should be based on the job activity and potential for exposure to the eyes and face.

Skin Protection: Use gloves or other appropriate personal protective equipment if skin contact with formulation is possible. Wear lab coat or other protective over garment if splashing is possible. The choice of protection should be based on the job activity and potential for skin contact.

Respiratory Protection: When possible, handle material in enclosed processes or containers. If it is properly handled with effective local exhaust ventilation or containment, respiratory protection may not be needed. For procedures involving larger quantities or dust/aerosol generating procedures such as weighing or a large transfer of liquids, an air-purifying respirator with NIOSH approval for dusts and mists may be needed. The choice of protection should be based on the job activity and the potential for exposure.

Other: Wash hands, face and other potentially exposed areas after handling material (especially before eating, drinking or smoking). Clean protective equipment thoroughly after each use.

8.3 Environmental exposure controls

Environmental Exposure Controls Avoid release to the environment.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	White to off-white (Drug for Injection)
Physical State:	Lyophilized powder
Molecular Weight:	719.91
Odor:	No information available
Odor Threshold:	No information available
pH:	3 - 4 following reconstitution
Melting Point:	No information available
Boiling Point:	No information available
Flash Point:	No information available
Evaporation Rate:	No information available
Lower explosive limit:	No information available
Upper explosive limit:	No information available
Vapor Pressure:	No information available
Vapor Density (air = 1):	No information available
Relative density:	No information available
Water Solubility:	2 mg/mL, following reconstitution with 29 mL water
Partition Coefficient (log Kow):	Log P: 3.77
Viscosity:	No information available

10. STABILITY AND REACTIVITY

10.1 Reactivity No information available

10.2 Chemical stability No information available

10.3 Possibility of hazardous reactions No information available

10.4 Conditions to avoid Carfilzomib, the active pharmaceutical ingredient in Kyprolis, will present an explosion and deflagration hazard risk when dispersed and ignited in air during manufacturing. Grounding and bonding of process equipment should be implemented. Consider inerting the process environment to mitigate an explosion hazard. High temperature process environments should be avoided to minimize the risk of a dust cloud explosion. This material is resistive and capable of accumulating a charge during process operations. It is recommended that measures are taken to reduce the rate of charge generation during transport. The rate of charge relaxation should also be increased by using proper bonding and grounding of process equipment.

10.5 Incompatible materials No information available

10.6 Hazardous decomposition products No information available

10.7 Other information Dust Explosion Hazard Properties tested on Carfilzomib -
MIE: 1mJ < MIE < 3 mJ (Es = 1.7) without inductance
MIT (dust cloud): 380°C
Kst: 318 bar-m/sec ± 10%
Pmax: 8.0 bar ± 10%
LOC: 12.5 vol % ± 1

Electrostatic Properties tested on Carfilzomib -
Volume resistivity: 4.0 x 10^{17} Ω-cm
Calculated Dielectric Constant: 2.4
Measured Decay Time: 84,960 sec

11. TOXICOLOGICAL INFORMATION

11.1 Information on toxicological effects

Acute Toxicity:	No information available
Skin corrosion/irritation:	No information available
Serious eye damage/eye irritation:	No information available
Respiratory or skin sensitization:	No information available
Germ cell mutagenicity:	Based on available data, the GHS classification criteria are not met.
Carcinogenicity:	No information available
Reproductive toxicity:	Based on available data, the GHS classification criteria are not met. The following carfilzomib information is available based on the intravenous route: In rats, there was an increase in pre-implantation loss and early resorptions at ≥ 1 mg/kg/day and maternal toxicity at ≥2 mg/kg/day. In rabbits, there was an increase in pre-implantation loss at ≥ 0.4 mg/kg/day and an increase in early resorptions and post-implantation loss and a decrease in fetal weight at the maternally toxic dose of 0.8 mg/kg/day.
STOT - single exposure:	Based on available data, the GHS classification criteria are not met. The following carfilzomib information is available based on the intravenous route of exposure. Four acute toxicity studies were conducted following IV exposure in animals (3 rats and 1 Cynomolgus monkeys). The single dose IV bolus administration of carfilzomib in rats resulted in significant toxicity at ≥7 mg/kg in rats and ≥ 1 mg/kg in Cynomolgus monkeys. Chymotrypsin-like proteasome activity inhibition was observed in whole blood, kidney, liver, heart, lung and adrenal at ≥1 mg/kg, with reversibility noted in tissues, but not blood.
STOT - repeated exposure:	Based on available data, the GHS classification criteria are not met. The following carfilzomib information is available based on the intravenous route of exposure. In repeat-dose toxicology studies, rats were administered bolus intravenous carfilzomib at 1, 2, or 4 mg/kg/day for 3 or 6 months, and monkeys were administered bolus intravenous carfilzomib at 0.5, 1, or 2 mg/kg/day (nine dosing cycles of 28 days: days 1-2, 8-9, and 15-16 of the 28 day cycle for 9 months). Many findings in nonclinical repeat-dose toxicity studies were related to the proteasome inhibition activities of carfilzomib, consisting of effects on hematological parameters (decreased platelets, increased red cell and white cell types) and hematopoietic organs (such as bone marrow, lymph nodes and spleen) in rats and monkeys. Both species had increased liver weights, serum CRP, neutrophils, monocytes, and fibrinogen and decreased alanine transaminase (ALT) and albumin in the chronic studies. In addition, significant toxicities were observed in the cardiovascular, gastrointestinal and renal systems.
Aspiration Hazard:	No information available

12. ECOLOGICAL INFORMATION

12.1 Toxicity

Ecotoxicity effects: No information available

12.2 Persistence and degradability

Persistence/Degradability: No information available

12.3 Bioaccumulative potential

Bioaccumulation/ Accumulation: No information available

12.4 Mobility in soil

Mobility in Environmental Media: No information available

12.5 Results of PBT and vPvB assessment

Results of PBT and vPvB assessment: No information available

12.6 Other adverse effects

Other Adverse Effects: No information available

13. DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

Waste Disposal Method: Dispose of waste according to prescribed federal, state, local and competent authority guidelines.

14. TRANSPORT INFORMATION

DOT Not regulated by U.S. DOT or IATA

15. REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

International Inventories

TSCA:	-
EINECS/ELINCS	-
DSL/NDSL	-
PICCS:	-
ENCS:	-
CHINA:	-
AICS:	-
KECL:	-

Legend
TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
PICCS - Philippines Inventory of Chemicals and Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
AICS - Australian Inventory of Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances

State Regulations

California Proposition 65: This product does not contain any Proposition 65 chemicals.

15.2 Chemical safety assessment

No CSA has been conducted.

16. OTHER INFORMATION

Text of R phrases mentioned in Section 2

No information available

Revision Number: 3

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active.