SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

General

Verastem, Inc.
117 Kendrick Street - Ste 500, Needham, MA 02494
Main: 781-292-4200
E-mail: sds@verastem.com

Emergency telephone number

ChemTel Inc. *(Available 24/7, 365 days/year):*
+1 (800) 255-3924 (US and Canada)
+01 (813) 248-0585 (International)
+1 (300) 954-583 (Australia)
0-800-591-6042 (Brazil)
400-120-0751 (China)
000-800-100-4086 (India)
01800-099-0731 (Mexico)

Product identifier

Duvelisib Capsules (5 mg, 15 mg, 25 mg)

Synonyms

IPI-145; VS-0145; INK-1197; duvelisib; (S)-3-(1-((9H-purin-6-yl)amino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one hydrate

Trade names

Copiktra

Chemical family

Phenylisoquinoline derivative

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

Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture packaged for use in clinical trials; under investigation to treat cancer

Note

This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical ingredient. The pharmacological, toxicological, and ecological properties of this ingredient have not been fully characterized. This SDS will be updated as more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. The classification and labeling listed below is for bulk drug product.

Globally Harmonized System [GHS]

Specific Target Organ Toxicity (repeated exposure) - Category 1. Aquatic toxicity (chronic) - Category 3.

Other/Supplemental

Mixture not yet fully tested

Label elements

GHS hazard pictogram

GHS signal word

Danger

GHS hazard statements

H372 - Causes damage to liver, hematopoietic, and lymphoid organs through prolonged or repeated exposure. H412 - Harmful to aquatic life with long lasting effects.

GHS precautionary statements

P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P314 - Get medical advice/ attention if you feel unwell. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations. P273 - Avoid release to the environment.

Other hazards

Duvelisib capsules contain duvelisib, a phosphoinositide 3 (PI3) kinase inhibitor. Commonly observed adverse effects in patients with blood cancers included rash, gastrointestinal (GI) upset (diarrhea, vomiting), markers of liver toxicity (ALT and AST increased), nausea, hematopoietic disturbances (low platelet, white, and red blood cell counts), cough, headache, fatigue, fever, and difficulty breathing. Effects subsided with drug cessation.

Note

This mixture/product is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
Microcrystalline Cellulose	9004-34-6	N/A	60-80%	Not classified
Duvelisib	1201438-56-3	N/A	5-15%	STOT-R1:H372; CA2: H411
Magnesium Stearate	557-04-0	209-150-3	0.5-1.5%	Not classified

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS …continued

Note	The ingredient(s) listed above are considered hazardous, or are listed because they have OELs and are present at ≥1%. The remaining components are not hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

Immediate Medical Attention Needed	Yes
Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11.
Indication of immediate medical attention and special treatment needed, if necessary	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, chloride, and nitrogen-containing compounds.

SECTION 5 - FIREFIGHTING MEASURES …continued

Flammability/ Explosivity	No information identified. High concentrations of finely divided airborne particles can potentially explode if ignited.
Advice for firefighters	In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	Do not open, crush, or break capsules. If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. Do not breathe dust.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	If capsules are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If capsules are crushed/broken, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Scoop up broken pieces. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	If capsules are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust. Wash thoroughly after handling.
Conditions for safe storage including any incompatibilities	Store at 15-30°C, away from incompatible materials.
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Note	Wash hands, face and other potentially exposed areas immediately in the event of physical contact.

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Microcrystalline Cellulose	OSHA	REL-TWA	10 mg/m³ (total); 5 mg/ m³ (respirable)
	ACGIH	TLV	10 mg/m³
	Netherlands	MAC-TGG	2 mg/m^3
	France	VME	10 mg/m³
Duvelisib	Verastem, Inc.	OEL	3 µg/m³
Magnesium Stearate	ACGIH	TWA-8 HR	10 mg/m³ (stearates)
	Lithuania	TWA-8 HR	3 mg/m³
	Sweden	TWA-8 HR	5 mg/m³

Exposure/Engineering controls

None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: Control exposures to below the OEL (if available). Otherwise, selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection

None required for normal handling of packaged product. If handling bulk product or capsules are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection

None required for normal handling of packaged product. If handling bulk product or capsules are crushed or broken: Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection

Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Eye/face protection	None required for normal handling of packaged product. If handling bulk product or capsules are crushed or broken: Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this mixture/product, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	capsule
Color	Commercial: White (5 mg), pink (15 mg), or white/orange (25 mg) Clinical: Orange (5 mg), white (25 mg)
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	Not applicable.
Flash point	No information identified.
Evaporation rate	Not applicable.
Flammability (solid, gas)	No information identified.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Vapor density	No information identified.
Relative density	No information identified.
Water solubility	No information identified.
Solvent solubility	No information identified..
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	Not applicable (Mixture)
Molecular weight	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	No information identified.
Possibility of hazardous reactions	Not expected to occur.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note	As limited data for the mixture were identified, the data below describe the active ingredient duvelisib.

Information on toxicological effects

Route of entry	May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Microcrystalline Cellulose	LD_{50}	Oral	Rat	>5 g/kg
	LC_{50} (4 hour)	Inhalation	Rat	>5800 mg/m^3
	LD_{50}	Dermal	Rabbit	> 2g/kg
Duvelisib	Maximum Tolerated Dose (MTD)	Oral	Monkey	>500 mg/kg
Magnesium Stearate	LC_{50}	Inhalation	Rat	>2000 mg/m³

Irritation/Corrosion Duvelisib was phototoxic in rats at high doses.

Sensitization No studies identified.

STOT-single exposure No adverse effects were noted following single oral dose of 500 mg/kg duvelisib in monkeys.

STOT-repeated exposure/Repeat-dose toxicity Repeat oral dose toxicity studies were carried out in rats and monkeys with duvelisib for up to 13 weeks of duration. Effects primarily occurred in the bone marrow and lymphoid tissues at ≥5 mg/kg/day, and were partially reversible in both species. Reversible GI and bladder toxicity (e.g. inflammation) also occurred in monkeys at ≥0.2 and ≥1 mg/kg/day, respectively. Reversible testicular toxicity was noted in rats at 25 mg/kg/day. Reversible changes in the liver and vascular were noted in some studies (further details not identified).

Reproductive toxicity No studies identified.

Developmental toxicity Oral administration of duvelisib to pregnant rats and rabbits during organogenesis caused resorptions, spontaneous abortion, and reduced fetal weight in the presence of excessive maternal toxicity. The NOAELs in rats and rabbits were 35 and 75 mg/kg/day, respectively.

Genotoxicity Duvelisib was not genotoxic *in vitro* (reverse bacterial mutagenicity assay, chromosomal abberation assay in human peripheral blood lymphocytes), or an *in vivo* bone marrow micronucleus test in rats treated with 350 mg/kg/day (highest dose tested).

Carcinogenicity No studies identified.

Aspiration hazard No studies identified

Human health data See "Section 2 - Other Hazards"

Additional information The toxicological properties of this mixture/product have not been fully characterized.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
Microcrystalline Cellulose	--	--	--
Duvelisib	NOEC/21 day	Daphnia Magna	0.44 mg/L
	EC_{50}/72h	Freshwater Alga	>3.4 mg/L
	NOEC/28 Day	Midge	181 mg/kg
Magnesium Stearate	--	--	--

Persistence and Degradability Conversion was low (<10%) in an aerobic transformation study (duvelisib).

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data available.

Note The environmental characteristics of this mixture/product have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods Used product should be disposed of according to local, state, and federal regulations. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines.

SECTION 14 - TRANSPORT INFORMATION

Transport Based on the available data, this mixture/product is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

UN number None assigned.

UN proper shipping name None assigned.

Transport hazard classes and packing group None assigned.

Environmental hazards Based on the available data, this mixture/product is not regulated as an environmental hazard or a marine pollutant.

SECTION 14 - TRANSPORT INFORMATION …continued

Special precautions for users	Mixture not fully tested - avoid exposure.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to liver, hematopoietic, and lymphoid organs through prolonged or repeated exposure. CA3 - Chronic Aquatic Toxicity Category 3. H412 - Harmful to aquatic life with long lasting effects. CA2 - Chronic Aquatic Toxicity Category 2. H411 - Toxic to aquatic life with long lasting effects.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level;

SECTION 16 - OTHER INFORMATION …continued

Abbreviations …continued	NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, bioaccumulative, and toxic substances; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
Issue Date	7 September 2018
Revisions	This is the first version of this SDS.
Disclaimer	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 is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.