

# SAFETY DATA SHEET

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

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### Contact information

#### General



Blueprint Medicines Corporation  
45 Sidney Street, Cambridge, MA 02139  
Main: +1 (617) 374-7580  
E-mail: info@blueprintmedicines.com

#### Emergency telephone number

+1 (617) 374-7580 (*Available M-F, 9 am - 5 pm EST*)

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### Product identifier

BLU-667 (Pralsetinib)

#### Synonyms

(cis)-N-((S)-1-(6-(4-Fluoro-1H-pyrazol-1-yl)pyridin-3-yl)ethyl)-1-methoxy-4-(4-methyl-6-(5-methyl-1H-pyrazol-3-ylamino)pyrimidin-2-yl)cyclohexanecarboxamide; BLU123244; X581238

#### Trade names

None identified

#### Chemical family

Modified aromatic

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

Active pharmaceutical ingredient (API); under investigation for the treatment of advanced solid tumors.

#### Note

This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical ingredient.

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## SECTION 2 - HAZARDS IDENTIFICATION

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### Classification of the substance or mixture

#### Globally Harmonized System [GHS]

Reproductive Toxicity - Category 2. Specific Target Organ Toxicity (repeated exposure) - Category 2.

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## SECTION 2 - HAZARDS IDENTIFICATION ...continued

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### Label elements

#### GHS hazard pictogram



#### GHS signal word

Warning

#### GHS hazard statements

H361d - Suspected of damaging the unborn child. H373 - May cause damage to cardiovascular, metabolic, skeletal, and hematopoietic systems through prolonged or repeated exposure.

#### GHS precautionary statements

P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust. P280 - Wear protective gloves/eye protection/face protection. P308 + P313 - If exposed or concerned: get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

#### Other hazards

BLU-667 is a selective inhibitor of Rearranged During Transfection (RET) kinase that is often mutated in different cancers. The most common adverse effects reported in patients included constipation, diarrhea, increased liver enzyme levels, fatigue, and headache.

The specificity of BLU-667 for mutated versus normal RET kinase is not known. RET signaling is critical for kidney development. Based on effects reported in animal studies in addition to its mechanism of action and off-target inhibitory properties, a potential for BLU-667 to adversely affect a developing fetus cannot be excluded in the absence of definitive data.

#### Note

This substance 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).

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## SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

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<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ ELINCS#</u>	<u>Amount</u>	<u>GHS Classification</u>
BLU-667	2097132-94-8	N/A	~100%	RT2: H361d; STOT-R2: H373

#### Note

The substance listed above is considered hazardous. See Section 16 for full text of GHS classifications.

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## SECTION 4 - FIRST AID MEASURES

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### 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

If swallowed, call a physician immediately. 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. Consult prescribing/packaging information.

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## SECTION 5 - FIREFIGHTING MEASURES

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#### 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, oxides of nitrogen and fluorine, and other nitrogen- or fluorine-containing compounds.

#### Flammability/Explosivity

No information identified. High concentrations of finely divided organic particles can 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.

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## SECTION 6 - ACCIDENTAL RELEASE MEASURES

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<b>Personal precautions, protective equipment and emergency procedures</b>	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Use only with adequate ventilation. Do not breathe dust.
<b>Environmental precautions</b>	Do not empty into drains. Avoid release to the environment.
<b>Methods and material for containment and cleaning up</b>	DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel to minimize entry of powder into the air. 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 regulations (see section 13). Decontaminate the area twice.
<b>Reference to other sections</b>	See Sections 8 and 13 for more information.

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## SECTION 7 - HANDLING AND STORAGE

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<b>Precautions for safe handling</b>	Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid breathing dust.
<b>Conditions for safe storage including any incompatibilities</b>	Store at room temperature between 59-86°F (15-30°C) away from light.
<b>Specific end use(s)</b>	Pharmaceutical.

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## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

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### Control Parameters/ Occupational Exposure Limit Values

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
BLU-667	--	--	--

<b>Exposure/Engineering controls</b>	Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust-generating points. Use specifically designed and engineered local exhaust ventilation (LEV) and/or enclosure at dust-generating points and for high dust-generating operations. Limited open handling allowable for low dust-generating operations. Emphasis is placed on closed material transfer through direct connections, dust control and containment using LEV, certified downflow booths, glove bags, process containment via intermediate bulk containers (IBCs) with split butterfly valves (SBVs) and/or isolator technology.
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**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**

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<b>Respiratory protection</b>	Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. At a minimum, a tight-fitting full-face respirator with HEPA filters is required when performing dust or aerosol generating operations. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required for spill cleanup.
<b>Hand protection</b>	Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.
<b>Skin protection</b>	Wear disposable coveralls appropriate to the task, booties, and safety glasses with side shields. Ensure gloves are protective against solvents in use. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of-doors. Employees must be trained in proper gowning and degowning practices.
<b>Eye/face protection</b>	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.
<b>Environmental Exposure Controls</b>	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.
<b>Other protective measures</b>	Wash hands in the event of contact with this substance, 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).

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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES**

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**Information on basic physical and chemical properties**

<b>Appearance</b>	Solid
<b>Color</b>	White to off-white
<b>Odor</b>	No information identified.
<b>Odor threshold</b>	No information identified.
<b>pH</b>	Not applicable
<b>Melting point/ freezing point</b>	~206°C
<b>Initial boiling point and boiling range</b>	No information identified.

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**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued**

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<b>Flash point</b>	No information identified.
<b>Evaporation rate</b>	No information identified.
<b>Flammability (solid, gas)</b>	No information identified.
<b>Upper/lower flammability or explosive limits</b>	No information identified.
<b>Vapor pressure</b>	No information identified.
<b>Vapor density</b>	No information identified.
<b>Relative density</b>	No information identified.
<b>Water solubility</b>	Insoluble (0.06 mg/mL at pH 7; 37°C)
<b>Solvent solubility</b>	Solubility in 50 mM USP buffer at 25°C: pH 4 (0.07 mg/L), pH 7 (0.06 mg/mL), and pH 10 (0.04 mg/mL). Solubility at 37°C in: 0.1 N HCl (1.61 mg/L), SGF (0.77 mg/mL), FaSSIF (0.05 mg/mL), and FeSSIF (0.07 mg/mL).
<b>Partition coefficient (n-octanol/water)</b>	No information identified.
<b>Auto-ignition temperature</b>	No information identified.
<b>Decomposition temperature</b>	No information identified.
<b>Viscosity</b>	No information identified.
<b>Explosive properties</b>	No information identified.
<b>Oxidizing properties</b>	No information identified.
<b>Other information</b>	
<b>Molecular formula</b>	C <sub>27</sub> H <sub>32</sub> FN <sub>9</sub> O <sub>2</sub>
<b>Molecular weight</b>	533.61 g/mol

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**SECTION 10 - STABILITY AND REACTIVITY**

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<b>Reactivity</b>	No information identified.
<b>Chemical stability</b>	Stable under recommended handling and storage conditions (See Section 7).
<b>Possibility of hazardous reactions</b>	No information identified.
<b>Conditions to avoid</b>	Avoid extreme temperatures.

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**SECTION 10 - STABILITY AND REACTIVITY ...continued**

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<b>Incompatible materials</b>	Strong oxidizing agents, strong acids, strong bases.
<b>Hazardous decomposition products</b>	No information identified.

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**SECTION 11 - TOXICOLOGICAL INFORMATION**

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**Information on toxicological effects**

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

**Acute toxicity**

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
BLU-667	--	--	--	--

**Irritation/Corrosion** BLU-667 did not cause lesions in the skin or eye of rats or monkeys.

**Sensitization** No studies identified.

**STOT-single exposure** No adverse effects were seen in rats treated with a single oral dose up to 300 mg/kg BLU-667. One monkey (out of three) at 300 mg/kg/day was found dead due to ulceration of the small and large intestines; single doses in monkeys up to 150 mg/kg/day were well-tolerated.

**STOT-repeated exposure/Repeat-dose toxicity** Repeated oral studies of up to 13 weeks were conducted with BLU-667 in rats (5 to 75 mg/kg/day) and monkeys (2 to 40 mg/kg/day). Rats exhibited effects in the hematopoietic system at all doses, and in the bone, teeth, and sex organs (*i.e.*, testis and ovary degeneration) at 20 mg/kg/day. Cardiovascular toxicity was noted at 75 mg/kg/day. Monkeys exhibited effects in the hematopoietic system at 10 mg/kg/day. Doses of 30 mg/kg/day and  $\geq 15$  mg/kg/day were lethal in rats and monkeys, respectively. The highest non-severely toxic dose (HNSTD) in rats was 20 mg/kg/day and in monkeys was 7.5 mg/kg/day.

**Reproductive toxicity** In a study with rats, no BLU-667-related findings were noted on male or female reproduction (mating, fertility, and pregnancy indices), estrous cyclicity, or spermatogenesis at any oral dose tested (up to 20 mg/kg/day; considered the reproductive a NOAEL).

**Developmental toxicity** Embryotoxicity (evidenced increased post-implantation loss and decreased embryo viability), and parental toxicity, was seen in a combination fertility and developmental toxicity study in rats treated orally with 20 mg/kg/day BLU-667. In a developmental toxicity study with pregnant rats, 100% post implantation losses (early resorptions) occurred at oral doses  $\geq 20$  mg/kg/day, while multiple malformations (absence of a kidney and ureter, malpositioned testis, and skeletal and soft tissue abnormalities) were noted at 5 and 10 mg/kg/day. A NOAEL for developmental toxicity was not identified.

**Genotoxicity** BLU-667 was negative for genotoxicity *in vitro* (Ames bacterial reverse mutation assay, micronucleus assay) and *in vivo* (micronucleus assay in rats).

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**SECTION 11 - TOXICOLOGICAL INFORMATION** ...continued

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<b>Carcinogenicity</b>	No studies identified.
<b>Aspiration hazard</b>	No studies identified
<b>Human health data</b>	See "Section 2 - Other Hazards"

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**SECTION 12 - ECOLOGICAL INFORMATION**

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<b>Toxicity</b>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
<u>Compound</u> BLU-667	--	--	--

**Persistence and Degradability** No data available.

**Bioaccumulative potential** No data available.

**Mobility in soil** No data available.

**Results of PBT and vPvB assessment** No data available.

**Other adverse effects** No data available.

**Note** The environmental characteristics of this substance have not been fully investigated. Releases to the environment should be avoided.

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**SECTION 13 - DISPOSAL CONSIDERATIONS**

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**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, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

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**SECTION 14 - TRANSPORT INFORMATION**

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**Transport** Based on the available data, this substance 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.



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**SECTION 14 - TRANSPORT INFORMATION ...continued**

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<b>Transport hazard classes and packing group</b>	None assigned.
<b>Environmental hazards</b>	Based on the available data, this substance is not regulated as an environmental hazard or a marine pollutant.
<b>Special precautions for users</b>	Due to lack of data, avoid release to the environment.
<b>Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code</b>	Not applicable.

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**SECTION 15 - REGULATORY INFORMATION**

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<b>Safety, health and environmental regulations/legislation specific for the substance or mixture</b>	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.
<b>Chemical safety assessment</b>	Not conducted.
<b>TSCA status</b>	Drugs are exempt from TSCA.
<b>SARA section 313</b>	Not listed.
<b>California proposition 65</b>	Not listed.
<b>Additional information</b>	No other information identified.

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**SECTION 16 - OTHER INFORMATION**

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<b>Full text of H phrases and GHS classifications</b>	H361d - Suspected of damaging the unborn child. RT2 - Reproductive toxicity Category 2. H373 - May cause damage to cardiovascular, metabolic, and hematopoietic systems through prolonged or repeated exposure. STOT-R2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2.
<b>Sources of data</b>	Information from published literature and internal company data.
<b>Abbreviations</b>	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 -

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**SECTION 16 - OTHER INFORMATION ...continued**

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**Abbreviations  
...continued**

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; 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; 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**

29 April 2020

**Revisions**

Updated data in Sections 1, 9, and 11; Updated labeling information.

**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.