

# MATERIAL SAFETY DATA SHEET

## MLN518

### Section 1 – Identification of the Substance and Company

#### SUBSTANCE IDENTIFICATION

**Product Name:** MLN518  
**Synonyms:** CT53518  
**Chemical Family:** FLT3 receptor tyrosine kinase inhibitor  
**Intended Use:** Active pharmaceutical ingredient

#### COMPANY IDENTIFICATION

Millennium Pharmaceuticals, Inc.  
40 Landsdowne Street  
Cambridge, MA 02139

In case of Emergency, contact: Chemtrec 1-800-424-9300

### Section 2 – Composition / Information on Ingredients

<u>Substance</u>	<u>CAS No.</u>	<u>EINECS/ELINCS No.</u>	<u>% (by wt)</u>	<u>EU Classification</u>
MLN518	Not assigned	Not assigned	> 99 %	Xn, R22, R48/22

### Section 3 – Hazards Identification

**Appearance:** White to yellow powder

**Signal Word:** CAUTION

**Hazard Overview:** Pharmacologically active compound currently under development as an anti-cancer treatment. The physical, chemical, and ecological properties of this material have not been fully characterized. Exposure by any route should be minimized. Exercise due care: wear suitable protective clothing, gloves and eye/face protection.

**Statement of Known Hazard:** Harmful by ingestion. Inhalation absorption assumed to be high. May be a bone marrow, liver and reproductive system toxicant.

**EU Indicator of Danger:** Xn, Harmful

#### **EU Risk Phrases:**

R 22 Harmful if swallowed.  
R 48/22 Harmful: danger of serious damage to health by prolonged exposure if swallowed.

## **Section 4 – First Aid Measures**

### **Eye Contact**

Immediately flush eyes thoroughly with water for at least 15 minutes; Seek immediate medical assistance and notify supervisor.

### **Skin Contact**

Remove all contaminated clothing and rinse area thoroughly with soap and water for 15 minutes; Seek immediate medical assistance and notify supervisor.

### **Inhalation**

Remove from exposure source; notify medical personnel and supervisor if breathing difficulties develop. Administer artificial respiration if necessary.

### **Ingestion**

Seek immediate medical assistance. Do not induce vomiting, give liquids, or use any other method to remove poison unless advised by physician or Poison Control

### **Medical Conditions Aggravated by Exposure**

No information available.

### **Notes to Physician**

MLN518 is a small molecule inhibitor of type III receptor tyrosine kinases, which include FLT3, PDGFR, c-Kit, and CSF-1R.

## **Section 5 – Fire Fighting Measures**

### **Flammability/Explosivity**

Not considered to be a fire hazard. No explosivity data available. High concentrations of finely divided airborne organic particles can potentially explode if ignited.

### **Extinguishing Media**

Water, alcohol foam, dry chemical, CO<sub>2</sub>

### **Special Fire Fighting Procedures**

Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

### **Hazardous Combustion Products**

Carbon monoxide and nitrogen oxides.

## **Section 6 – Accidental Release Measures**

### **Spill Protection Equipment**

For large spill wear a respirator or other device that will protect you from dust or aerosols raised during the spill. Wear safety goggles, water-resistant coveralls, rubber boots and heavy rubber gloves.

### **Procedures to be Followed in Case of Leak or Spill**

If in liquid form, surround spill using spill pillows or other absorbents. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.

If in solid or dried form, do not raise dust. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize powder from entering the air. Add excess liquid to allow for the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.

## **Section 7 – Handling and Storage**

### **Storage**

Store in a well-ventilated area at controlled room temperature and away from sources of ignition and incompatible materials. Protect against physical damage.

### **Other Precautions**

Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personnel protective equipment if needed). Wash thoroughly after handling.

## **Section 8 – Exposure Controls / Personal Protection**

### **Occupational Exposure Limit / Occupational Exposure Category or Band**

None currently established by OSHA, NIOSH or ACGIH. Millennium considers the active pharmaceutical ingredient to be **moderate to highly toxic and potent** because of the potential for this compound to cause bone marrow, liver and reproductive system toxicity, and based on compounds with a similar pharmacological mechanism.

### **Engineering Controls**

When practicable, handle material in enclosed processes or in processes with effective and well-engineered local exhaust ventilation. The emphasis of control should be on little, if any, open handling and containment and control at the source of dust or aerosol generation. For re-constitution, the lyophilized powder should be handled in a ventilated enclosure, Biological Safety Cabinet, a barrier isolator, or other equivalent containment device.

### **Eye Protection**

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.

### **Respiratory Protection**

- When possible, handle material in enclosed processes or containers. For reconstitution, when feasible, handle in a ventilated balance enclosure, Biological Safety Cabinet, a barrier isolator or other equivalent containment device using good work practices to contain product within these devices. In the laboratory, if it is properly handled with effective containment, respiratory protection may not be needed.
- If conducting activities outside of containment where there is a potential for aerosolization of the drug product, use of an air-purifying respirator with NIOSH approval for dusts and mists should be considered.

### **Skin Protection**

Rubber gloves are recommended to minimize potential for skin contact when handling in dry form or in aqueous solutions. Double gloves should be considered. When the material is dissolved in an organic solvent, wear gloves that provide protection against the solvent. Wear lab coat or other protective overgarment. Base the choice of protection on the job activity and potential for skin contact.

**Other**

Wash hands, face and other potentially exposed areas immediately after handling material (especially before eating, drinking, or smoking). Decontaminate all protective equipment after use. Exercise extreme care when working with sharps/needles/syringes and potent drugs.

**Section 9 – Physical/Chemical Properties**

<b>Physical State:</b>	Solid (powder)
<b>Color:</b>	White to yellow
<b>Molecular Formula:</b>	C <sub>31</sub> H <sub>42</sub> N <sub>6</sub> O <sub>4</sub>
<b>Molecular Weight:</b>	563
<b>pH:</b>	Not applicable
<b>Boiling Point:</b>	Not determined
<b>Melting Point:</b>	Not determined
<b>Vapor Pressure:</b>	Not determined
<b>Solubility in Water:</b>	Not determined
<b>Evaporation Rate:</b>	Not applicable
<b>Specific Gravity:</b>	Not determined
<b>Vapor Density:</b>	Not determined
<b>Percent Volatile:</b>	Not determined

**Section 10 – Stability/Reactivity**

<b>Stability:</b>	Pharmacologically stable
<b>Incompatibility:</b>	May be slightly hygroscopic
<b>Hazardous Polymerization:</b>	Not known to occur
<b>Hazardous Decomposition Products:</b>	None expected
<b>Conditions to Avoid:</b>	Not known

**Section 11 – Toxicological Information****Acute Toxicity:**

LD50 oral, rat: >300, <1000 mg/kg.

**Repeat Dose Toxicity:**28 day oral studies:

Well tolerated up to 100 mg/kg BID in rats and up to 10 mg/kg BID in dogs. Compound-related effects on the bone marrow and related hematological effects were observed at ≥60 mg/kg/day in rats and predominantly at 20 mg/kg/day in dogs. In addition, rats exhibited increases in plasma transaminases, alkaline phosphatase, creatinine, cholesterol and BUN at ≥60 mg/kg/day. Lastly, ovarian luteal hemorrhages and /or luteal cysts were observed in female rats at ≥20 mg/kg/day; the toxicological significance of these changes is uncertain.

90 day oral studies:

Minimal to mild liver toxicity (hepatobiliary lesions with elevated liver enzymes) were noted in dogs given 10 mg/kg BID. Effects were reversible after 28 days. No effects were seen at 3 mg/kg BID.

**Irritation/Sensitization:**

No data available

**Genotoxicity:**

Negative in the Ames bacterial mutagenicity assay, the mouse lymphoma assay and rat micronucleus assay.

**Carcinogenicity:**

No data available

**Reproductive and Developmental Toxicity:**

No data available

**Human Clinical Data**

MLN518 has been evaluated to date in a single phase I/II clinical trial in patients with acute myelogenous leukemia at a clinical dose of 525 and 700 mg BID orally. MLN518 has been associated with dose-related nausea, vomiting, and diarrhea. Occasional patients have also been noted to develop peripheral edema. Patients with high systemic exposure to MLN518 have experienced generalized muscular weakness, including in one patient bilateral ptosis (eyelid weakness). This weakness has been universally reversible upon cessation of MLN518 administration.

**Section 12 – Ecological Information****Persistence and Degradability**

No data available.

**Aquatic Toxicity**

No data available.

**Section 13 – Disposal Considerations**

All wastes containing the material should be properly labeled. Dispose of any waste residues according 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.

**Section 14 – Transport Information**

Transport according to all local, state and federal regulations.

**Hazard Class:** Not regulated

**UN Number:** Not applicable

**Section 15 – Regulatory Information**

**US OSHA:** This MSDS complies with the requirements under 29 CFR 1910.1200

Containers of this material should have affixed the following label (in addition to the identity label):

**OSHA Label**

Toxic; Affects the bone marrow; Affects the liver; May affect the reproductive system

**DANGER:** Pharmacologically active compound currently under development as an anti-cancer treatment. The physical, chemical, and ecological properties of this material have not been fully

characterized. Exposure by any route should be minimized. Read and understand the Material Safety Data Sheet before handling material.

**EU Indication of Danger**

Xn Harmful

**EU Hazard Symbol:**



**EU Risk Phrases**

R 22 Harmful if swallowed.  
R 48/22 Harmful: danger of serious damage to health by prolonged exposure if swallowed.

**EU Safety Phrases**

S 53 Avoid exposure – Obtain special instructions before use

**Canada – WHMIS Classifications**

Drugs are exempt, however, if not a drug, the most appropriate classification for MLN518 would be Class D, Division 2, Subdivision A; based on its potential to be a developmental and liver toxicant.

**California Proposition 65**

Not listed.

- SARA 313:** Not listed.
- CERCLA :** Not listed.
- RCRA:** Not listed.
- TSCA:** Not listed.
- Other:** Not listed.

**Section 16 – Other Information**

No additional information.

This MSDS supercedes the previous version dated 04-25-03.

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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 potent pharmaceutical product.