



# Vincristine Sulfate Injection

Effective Date: 05-May-2000

Eli Lilly and Company  
Material Safety Data Sheet

## Section 1 - Chemical Product and Company

**Manufacturer:**  
Eli Lilly and Company  
Lilly Corporate Center  
Indianapolis, IN 46285

**Manufacturer's Emergency Phone:**  
1-317-276-2000  
**CHEMTREC:**  
1-800-424-9300 (North America)  
1-703-527-3887 (International)

**Common Name:** Vincristine Sulfate Injection

**Chemical Name:** Vincal leukoblastine, 22-oxo-, sulfate(1:1) (salt)

**Synonym(s):** 037050 Formulation; Vincristine Sulfate; Vincristine; Vincristine Sulfate Formulation; 037231 Formulation; LCR Injection; VCR Injection; Vincrisul; Vincristina; Leurocristine

**Trademarks(s):** Oncovin

**Lilly Item Code(s):** HY7198; HY7199; VF0173; VF0174; VF0175; VL7194; VL7195; VL7196

See attached glossary for abbreviations.

## Section 2 - Composition / Information on Ingredients

<u>Ingredient</u>	<u>CAS</u>	<u>Concentration %</u>
Vincristine Sulfate	2068-78-2	0.1
Water	7732-18-5	> 99

Contains no hazardous components (one percent or greater) or carcinogens (one-tenth percent or greater) not listed above.

**Exposure Guidelines:**

Vincristine sulfate - LEG 0.14 micrograms/m<sup>3</sup> TWA for 12 hours. Excursion Limit 1.68 micrograms/m<sup>3</sup> for no more than a total of 30 minutes.

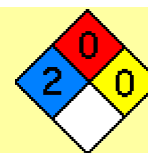
## Section 3 - Hazards Identification

**Appearance:** Colorless liquid

**Physical State:** Liquid

**Odor:** Very faint vinegar-like

## Emergency Overview



Special  
R = Reproductive

**Emergency Overview Effective Date:** 14-Aug-1998

### Lilly Laboratory Labeling Codes:

**Health** 2

**Fire** 0

**Reactivity** 0

**Special** R

**Primary Physical and Health Hazards:** Irritant (eyes, skin). Reproductive, Blood and Bone Marrow Effects.

**Caution Statement:** Vincristine Sulfate Injection may be irritating to the eyes and skin. Effects of exposure may include decreased fertility, fetal changes, decreased blood cell counts, bone marrow changes.

**Routes of Entry:** Inhalation and skin absorption.

**Effects of Overexposure:** Major anti-tumor activity, with vincristine sulfate is when administered to patients intravenously, is to arrest cell mitosis. It has subtle effects on nucleic acid synthesis, but not on nucleic acid function.

In the manufacturing setting, vincristine sulfate has been reported to be a skin irritant. Black workers have experienced depigmentation.

Accidental contamination of the eye in the manufacturing setting and in clinical settings results in severe irritation, tearing, pain, and blurred vision. Healing occurs within two weeks without loss of vision. In laboratory animals, "pitting" of the cornea has occurred after direct application of vincristine to the eye. Pitting may be delayed but can heal without loss of vision. If delivered under pressure, corneal ulceration has occurred in these animals.

**NOTE TO PHYSICIAN:** Vinca alkaloids do not cause a direct chemical burn of eye tissue, but interfere with the reproduction of the eye epithelium, which occurs continuously. The result is a delayed burn and subsequent scarring. While very painful, all cases have recovered completely without any loss of eye function.

Some patients treated with combination therapy which included vincristine sulfate have developed second malignancies.

The available data are insufficient to evaluate the mutagenic or chromosomal effects of vincristine sulfate in humans.

Some patients treated with combination therapy which included vincristine sulfate have had a decrease in fertility.

The vincristine sulfate is embryotoxic and teratogenic in animals. There have been no clinical trials in humans to determine if vincristine sulfate causes malformations of the human fetus. Information on the use of vincristine sulfate during human pregnancy is limited. There are individual case reports of normal infants born to patients treated while pregnant with vincristine sulfate in combination with other drugs for acute leukemia. Most, but not all, of these patients were treated during the second and third trimesters. There are individual case reports of normal and abnormal infants born to patients treated with vincristine sulfate alone and in combination with other drugs in the first trimester.

There have been no studies to determine whether immune suppression occurs in workers handling vincristine sulfate. At intravenous doses which suppress bone marrow function, weak immune suppression has occurred in a few patients; the major adverse effects in patients treated intravenously relate to the peripheral nervous system.

Inhalation of a sufficient amount of vincristine powder or vincristine sulfate would be expected to cause local irritation of the nose and throat. The vincristine sulfate is not dependably absorbed after oral administration. The systemic effect of accidental or intentional ingestion or inhalation would be variable, depending upon the amount absorbed.

Hospital employees and health care providers who prepare many cytostatic drugs in an unprotected environment have been reported to have increased levels of mutagens in their urine. The significance of this finding is not known.

**Medical Conditions Aggravated by Exposure:** In clinical use, patients with Charcot-Marie-Tooth Syndrome should not receive Oncovin. In the workplace, workers with neuromuscular dysfunction or sensitivity to vincristine sulfate should not be exposed to vincristine sulfate.

**Carcinogenicity:**

Vincristine sulfate - IARC Group 3 (not classifiable as to human carcinogenicity). Not listed by NTP, ACGIH, or OSHA.

## Section 4 - First Aid Measures

The vincristine sulfate is a cytotoxic material.

**Eyes:** Hold eyelids open and flush with a steady, gentle stream of water for 15 minutes. See an ophthalmologist (eye doctor) or other physician immediately.

**NOTE TO PHYSICIAN:** A steroid eye ointment or drops serve to minimize inflammation.

**Skin:** Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with plenty of soap and water. Get medical attention if irritation develops.

**Inhalation:** Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

**Ingestion:** Contact physician immediately for observation. Nausea and vomiting may result.

**Notes to Physician:** There are no published clinical data on the consequences of oral ingestion of vincristine. Should oral ingestion occur, the stomach should be evacuated. Evacuation should be

followed by oral administration of activated charcoal and a cathartic.

## Section 5 - Fire Fighting Measures

**Flash Point:** No applicable information found

**UEL:** No applicable information found

**LEL:** No applicable information found

**Extinguishing Media:** Use water, carbon dioxide, dry chemical, foam, or Halon.

**Unusual Fire and Explosion Hazards:** None known.

**Hazardous Combustion Products:** May emit toxic fumes when exposed to heat or fire.

## Section 6 - Accidental Release Measures

**Spills:** Use double pairs of latex disposable gloves which must be disposed of within an hour, goggles, impermeable body covering, and approved HEPA-filtered or supplied-air respirator. If material spills occur in production area, use either wet clean-up methods, ensuring that no airborne dusts or aerosols are formed, or appropriate vacuum cleaners having high efficiency particulate air (HEPA) filters.

It is recommended that areas handling final finished product have cytotoxic spill kits available. Spill kits should include impermeable body covering, shoe covers, latex and utility latex gloves, goggles, approved HEPA respirator, disposable dust pan and scoop, absorbent towels, spill control pillows, disposable sponges, sharps container, disposable garbage bag, and a hazardous waste label.

Material may be decomposed using a basic (pH of approximately 10) sodium hypochlorite solution.

## Section 7 - Handling and Storage

**Storage Conditions:** Refrigerator: 2 to 8 C (36 to 46 F).

## Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

For appropriate handling precautions in specific laboratory, manufacturing, or clinical health care operations, consult with a health and safety or technical services representative.

In clinical health care settings, follow OSHA Technical Manual, Section VI, Chapter 2 - Controlling Occupational Exposure to Hazardous Drugs. This chapter covers protection of employees during cytotoxic drug preparation, administration, disposal, and the handling of human waste products potentially contaminated with cytotoxic drug substances.

**GENERAL:** For all work environments, wear eye protection and ELIMINATE hand-to-eye contact. Avoid skin contact, wear gloves, and take other appropriate precautions.

**Respiratory Protection:** When the exposure guidelines may be exceeded, use an approved HEPA-filtered or supplied-air respirator.

**Eye Protection:** Chemical goggles and/or face shield.

**Ventilation:** Extensive local exhaust, ventilated enclosure (HEPA-filtered balance enclosure, fume hood, or Class II or III vertical flow biosafety cabinet), or enclosed process equipment.

**Other Protective Equipment:** Chemical-resistant gloves and impermeable body covering to minimize skin contact. If handled in a ventilated enclosure, as in a laboratory setting, respirator and goggles or face shield may not be required. Safety glasses are always required.

**Additional Exposure Precautions:** In production settings, airline-supplied, hood-type respirators are preferred. Shower and change clothing if skin contact occurs.

## Section 9 - Physical and Chemical Properties

**Appearance:** Colorless liquid

**Odor:** Very faint vinegar-like

**Boiling Point:** 100 C (212 F)

**Melting Point:** Not applicable

**Specific Gravity:** Approximately 1.00

**pH:** 3.5-5.5

**Evaporation Rate:** No applicable information found

**Water Solubility:** Soluble

**Vapor Density:** No applicable information found

**Vapor Pressure:** No applicable information found

## Section 10 - Stability and Reactivity

**Stability:** Stable at normal temperatures and pressures.

**Incompatibility:** None known.

**Hazardous Decomposition:** May emit toxic fumes when heated to decomposition.

**Hazardous Polymerization:** Will not occur.

## Section 11 - Toxicological Information

### Acute Exposure

Toxicity data for vincristine sulfate injection and vincristine sulfate are reported as indicated.

#### Oral:

Vincristine sulfate injection - Rabbit, 1000 mg/kg, no deaths or toxicity.

**Skin:**

Vincristine sulfate injection - Rabbit, 1000 mg/kg, no deaths or toxicity.

**Inhalation:**

Vincristine sulfate - Rat, 1200 mg/m<sup>3</sup> for 1 hour, no deaths or toxicity.

**Intravenous:**

Vincristine sulfate - Rat, median lethal dose 1 mg/kg, reduced activity, diarrhea, drooping eyelids, increased urine output, labored breathing, body weight loss.

Mouse, median lethal dose between 1.3 mg/kg and 3.4 mg/kg, coma, paralysis, tremors, lethargy, drooping eyelids, reduced activity, uncoordinated hindlimb movements.

**Skin Contact:**

Vincristine sulfate injection - Rabbit, slight irritant

**Eye Contact:**

Vincristine sulfate injection - Rabbit, slight irritant

## Chronic Exposure

Toxicity data for the active ingredient, vincristine sulfate, are reported.

**Target Organ Effects:**

Vincristine sulfate - Bone marrow suppression, blood effects (decreased red and white blood cell count), liver effects (increased liver enzymes).

**Other Effects:**

Vincristine sulfate - Weakness, anorexia, tremors, incoordination, diarrhea, lethargy.

**Reproduction:**

Vincristine sulfate - Decreased fertility, fetal death, embryotoxicity, skeletal defects.

**Sensitization:** No applicable information found.

**Mutagenicity:**

Vincristine sulfate - Not considered mutagenic in bacterial or mammalian cells.

## Section 12 - Ecological Information

No applicable ecological information found.

## Section 13 - Disposal Considerations

**Waste Disposal:** To avoid accidental exposure due to waste handling, place waste residue in a segregated, sealed plastic container. Used syringes, needles, and sharps should not be crushed, clipped, or recapped, but placed directly into an approved sharps container. Dispose of any cleanup materials and waste residue according to all applicable laws and regulations, e.g., secure chemical landfill disposal. The vinca alkaloids are natural products and are biodegradable. If disposed of by incineration,

a temperature of at least 850 C (1562 F) for solids is required and a temperature of at least 950 C (1742 F) for liquids is required.

## Section 14 - Transport Information

### Regulatory Organizations:

**DOT:** Not Regulated

**ICAO/IATA:** Not Regulated

**IMO:** Not Regulated

## Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Eli Lilly and Company usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

### U.S. Regulations

Vincristine sulfate

TSCA - No

CERCLA - Not on this list.

SARA 302 - Not on this list.

SARA 313 - Not on this list.

OSHA Substance Specific - No

California Proposition 65 (Cancer/Reproductive) - Name on developmental toxin list is vincristine sulfate.

### EU Regulations

#### EC Classification

Xn (Harmful)

Xi (Irritant)

Reproductive Category 3

#### Risk Phrases

R 22 - Harmful if swallowed.

R 36/38 - Irritating to eyes and skin.

R 62 - Possible risk of impaired fertility.

R 63 - Possible risk of harm to the unborn child.

R 68/22 - Harmful: possible risk of irreversible effects if swallowed.

#### Safety Phrases

S 24 - Avoid contact with skin.

S 35 - This material and its container must be disposed of in a safe way.

S 36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

S 53 - Avoid exposure -- obtain special instructions before use.

## Section 16 - Other Information

**MSDS Sections Revised:** Sections 1, 2, 3, 5, 7, 8, 9, 10, 11, 12, and 15.

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:

Eli Lilly and Company  
Hazard Communication  
317-277-6029

For additional copies contact:

Eli Lilly and Company  
1-800-LILLY-Rx (1-800-545-5979)

### GLOSSARY:

ACGIH = American Conference of Governmental Industrial Hygienists

AIHA = American Industrial Hygiene Association

BEI = Biological Exposure Index

CAS Number = Chemical Abstract Service Registry Number

CERCLA = Comprehensive Environmental Response Compensation and Liability Act (of 1980)

CHAN = Chemical Hazard Alert Notice

CHEMTREC = Chemical Transportation Emergency Center

DOT = Department of Transportation

EC = European Community

EINECS = European Inventory of Existing Chemical Substances

ELINCS = European List of New Chemical Substances

EPA = Environmental Protection Agency

HEPA = High Efficiency Particulate Air (Filter)

IARC = International Agency for Research on Cancer

ICAO/IATA = International Civil Aviation Organization/International Air Transport Association

IEG = Lilly Interim Exposure Guideline

IMO = International Maritime Organization

Kow = Octanol/Water Partition Coefficient

LEG = Lilly Exposure Guideline

LEL = Lower Explosive Limit

MSDS = Material Safety Data Sheet

MSHA = Mine Safety and Health Administration

NA = Not Applicable, except in Section 14 where NA = North America

NADA = New Animal Drug Application

NAIF = No Applicable Information Found  
NCI = National Cancer Institute  
NIOSH = National Institute for Occupational Safety and Health  
NOS = Not Otherwise Specified  
NTP = National Toxicology Program  
OSHA = Occupational Safety and Health Administration  
PEL = Permissible Exposure Limit (OSHA)  
RCRA = Resource Conservation and Recovery Act  
RQ = Reportable Quantity  
RTECS = Registry of Toxic Effects of Chemical Substances  
SARA = Superfund Amendments and Reauthorization Act  
STEG = Lilly Short Term Exposure Guideline  
STEL = Short Term Exposure Limit  
TLV = Threshold Limit Value (ACGIH)  
TPQ = Threshold Planning Quantity  
TSCA = Toxic Substances Control Act  
TWA = Time Weighted Average/8 Hours Unless Otherwise Noted  
UEL = Upper Explosive Limit  
UN = United Nations  
WEEL = Workplace Environmental Exposure Level (AIHA)