



Vinblastine Sulfate for Injection

Eli Lilly and Company
Material Safety Data Sheet

Effective Date: 18-May-2000

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: Vinblastine Sulfate for Injection

EC Number: 2056-06-0

Chemical Name: Vincal leukoblastine, sulfate (1:1) (salt)

Synonym(s): 039745 Formulation; VLB Formulation; Vinblastina Formulation; Vinca Alkaloid Formulation; Vinblastine Sulphate for Injection

Trademarks(s): Exal; Velbe; Velban

Lilly Item Code(s): AM0687; AM0755; VL0687; VL7095; VL7301

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

<u>Ingredient</u>	<u>CAS</u>
Vinblastine Sulfate	143-67-9

Exposure Guidelines:

Vinblastine sulfate - LEG 0.47 micrograms/m³ TWA for 12 hours. Excursion Limit 5.64 micrograms/m³ for no more than a total of 30 minutes.

Section 3 - Hazards Identification

Appearance: White to off-white powder

Physical State: Solid

Odor: Odorless

Emergency Overview



Special
R = Reproductive

Emergency Overview Effective Date: 18-May-2000

Lilly Laboratory Labeling Codes:

Health 3

Fire 1

Reactivity 1

Special R

Primary Physical and Health Hazards: Highly Toxic. Corrosive (eyes). Irritant (skin, respiratory tract). Reproductive, Blood and Bone Marrow Effects.

Caution Statement: Vinblastine Sulfate for Injection is highly toxic, may cause burns or permanent tissue damage to the eyes, and may be irritating to the skin and respiratory tract. Effects of exposure may include decreased fertility, fetal changes, changes in blood cell counts, and bone marrow changes.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Vinblastine sulfate's major anti-tumor activity, when administered to patients intravenously, is to arrest cell mitosis. It has subtle effects of nucleic acid synthesis, but not on nucleic acid function.

In the manufacturing setting, vinblastine sulfate powder and vinblastine sulfate have been reported to be skin irritants. 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 vinblastine 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 corneal 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 vinblastine sulfate have developed second malignancies.

The available data are insufficient to evaluate the mutagenic or chromosomal effects of vinblastine

sulfate in
humans.

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

Vinblastine sulfate is embryotoxic and teratogenic in animals. There have been no clinical trials in
humans to
determine if vinblastine sulfate causes malformations of the human fetus. Information on the use of
vinblastine sulfate during human pregnancy is limited. There are individual case reports of normal
infants
born to patients treated with vinblastine sulfate therapy alone for malignant disease throughout
pregnancy. There are individual case reports of abnormal infants born to patients treated in the first
trimester
with combination therapy which included vinblastine.

There have been no studies to determine whether immune suppression occurs in workers handling
vinblastine
sulfate. The major adverse effect in patients receiving intravenous doses of vinblastine sulfate relates to
reduced production of cells by the bone marrow.

No inhalation studies have been done on animals or humans. Inhalation of a sufficient amount of
vinblastine
powder or vinblastine sulfate powder would be expected to cause local irritation of the nose and
throat. Vinblastine sulfate is not dependably absorbed after oral administration to patients. 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: None known.

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

Section 4 - First Aid Measures

Vinblastine 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 ingestion of vinblastine. Should 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: As a finely divided material, may form dust mixtures in air which could explode if subjected to an ignition source.

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: Sub-Freezer: -50 C (-58 F) or colder. Chill Room: 2 to 8 C (36 to 46 F) for vials and ampules.

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: White to off-white powder

Odor: Odorless

Boiling Point: No applicable information found

Melting Point: Decomposes when heated above 210 C (410 F)

Specific Gravity: No applicable information found

pH: 3.5 to 5.0 (0.1% in 0.9% sodium chloride solution)

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: This material should not be exposed to temperatures above 125 C (257 F). This temperature is based on a laboratory test (Accelerated Rate Calorimetry) and assumes near atmospheric pressures and quantities of less than 500 kg (1100 lb). For additional information refer to the CHL data base on ELVIS or contact the Lilly Chemical Hazards Laboratory.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.) and strong bases.

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

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

Oral: Rat, median lethal dose 7 mg/kg, increased urine output, diarrhea, weight loss.

Skin: Rabbit, 1 mg/kg, no deaths or toxicity.

Inhalation: No applicable information found.

Intravenous: Rat, median lethal dose between 1.4 mg/kg and 4.4 mg/kg, anorexia, diarrhea, increased urine output, dehydration, reduced activity, weight loss.

Skin Contact: Rabbit, slight irritant

Eye Contact: Rabbit, corrosive

Chronic Exposure

Target Organ Effects: Nervous system effects (coma), heart effects (decreased blood pressure), blood effects (decreased white blood cell count), respiratory effects (respiratory failure), bone marrow effects (bone marrow hyperplasia, decreased bone marrow myeloid cell count).

Other Effects: Body weight loss, diarrhea, decreased food intake.

Reproduction: Decreased fertility, decreased fetal survival, skeletal defects.

Sensitization: No applicable information found.

Mutagenicity: Not 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:

Proper Shipping Name: Medicines, solid, toxic, n.o.s. (vinblastine sulfate)

UN/NA: UN3249

Hazard Class: 6.1

Packing Group: II

ICAO/IATA:

Proper Shipping Name: Medicine, solid, toxic, n.o.s. (vinblastine sulfate)

UN/NA: UN3249

Hazard Class: 6.1

Packing Group: II

IMO:

Proper Shipping Name: Medicine, solid, toxic, n.o.s. (vinblastine sulfate)

UN/NA: UN3249

Hazard Class: 6.1

Packing Group: II

This material in final packaged form may be shipped under the Consumer Commodity exception by Highway within the United States under limited circumstances. Please contact your local Hazardous Material/Dangerous Goods representative for the proper use of this exception.

Additional Information: Label(s): 6.1

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

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 development toxin list is vinblastine

sulfate.

EU Regulations

EC Classification

T+ (Very Toxic)

Xn (Harmful)

Xi (Irritant)

Reproductive Category 3

Risk Phrases

R 28 - Very toxic if swallowed.

R 37/38 - Irritating to respiratory system and skin.

R 41 - Risk of serious damage to eyes.

R 62 - Possible risk of impaired fertility.

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

Safety Phrases

S 26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

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

S 45 - In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

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

Section 16 - Other Information

MSDS Sections Revised: New MSDS.

Emergency Overview Sections Revised: New caution.

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

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)