



Gemcitabine Hydrochloride for Injection

Eli Lilly and Company
Material Safety Data Sheet

Effective Date: 22-Sep-2005

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: Gemcitabine Hydrochloride for Injection

Chemical Name: Cytidine, 2'-deoxy-2',2'-difluoro-, monohydrochloride

Chemical Name 2: 2'-Deoxy-2',2'-difluorocytidine monohydrochloride (beta-isomer)

Synonym(s): Gemcitabine HCl formulation; Gemcitabine; 264368 formulation; 188011 hydrochloride formulation

Trademarks(s): Gemcin; Gemtro; Gemzar

Lilly Item Code(s): VL7501; VL7502; VL7538; VL7540

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Gemcitabine Hydrochloride	122111-03-9	51 - 53
Excipients	NA	47 - 49

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

Exposure Guidelines:

Gemcitabine hydrochloride - LEG 0.3 micrograms/m³ TWA for 8 hours, LEG 0.2 micrograms/m³ TWA for 12 hours. Excursion guidance is to maintain full shift TWA.

Section 3 - Hazards Identification

Appearance: White to off-white powder or freeze-dried plug

Physical State: Solid

Odor: Odorless

Emergency Overview



Special
R = Reproductive

Emergency Overview Effective Date: 29-Oct-1998

Lilly Laboratory Labeling Codes:

Health 2

Fire 1

Reactivity 0

Special R

Primary Physical and Health Hazards: Skin Permeable. Mutagen. Irritant (eyes, skin).
Reproductive and Blood Effects.

Caution Statement: Gemcitabine Hydrochloride for Injection contains gemcitabine hydrochloride which may enter the body through the skin, alters genetic material, and may be irritating to the eyes and skin. Effects of exposure may include decreased fertility, fetal changes, and decreased blood cell counts.

Routes of Entry: Inhalation and skin absorption.

Effects of Overexposure: Based on animal data, gemcitabine hydrochloride for injection may be absorbed through the skin in amounts capable of producing systemic toxicity and may be irritating to the eyes and skin. Effects of exposure due to therapeutic use may include, but are not limited to, decreased blood cell counts, nausea, vomiting, edema, rash, elevated liver enzymes, and flu-like syndrome.

Medical Conditions Aggravated by Exposure: None known.

Carcinogenicity: No carcinogenicity data found. Not listed by IARC, NTP, ACGIH, or OSHA.

Section 4 - First Aid Measures

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.

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: Do not induce vomiting. Call a physician or poison control center. If available, administer activated charcoal (6-8 heaping teaspoons) with two to three glasses of water. Do not give anything by mouth to an unconscious person. Immediately transport to a medical care facility and see a physician.

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 chloride and fluoride 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.

Section 7 - Handling and Storage

Storage Conditions: Controlled Room Temperature: 15 to 30 C (59 to 86 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, 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 or freeze-dried plug

Odor: Odorless

Boiling Point: Not applicable

Melting Point: No applicable information found

Density: No applicable information found

pH: Acidic

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

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

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Oral:

Gemcitabine hydrochloride - Rat, 500 mg/kg, no deaths.

Mouse, mortality due to intestinal lesions reported when given a single dose of 333 mg/kg and higher.

Skin:

Gemcitabine hydrochloride for injection - Rabbit, median lethal dose estimated greater than 1000 mg/kg, mortality, reduced activity, diarrhea, weight loss, few feces, pale eyes, salivation.

Inhalation: No applicable information found.

Skin Contact:

Gemcitabine hydrochloride for injection - Rabbit, irritant

Eye Contact:

Gemcitabine hydrochloride - Rabbit, irritant

Chronic Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Target Organ Effects:

Gemcitabine hydrochloride - Blood effects (decreased red blood cell, white blood cell, and platelet counts).

Reproduction:

Gemcitabine hydrochloride - Decreased sperm formation and decreased fertility in males, and reproductive tissue changes. Depressed fetal viability and weight and malformations at doses toxic to the mother.

Sensitization:

Gemcitabine hydrochloride - Guinea pig, subcutaneous, negative systemic response.

Mutagenicity:

Gemcitabine hydrochloride - Mutagenic in mouse lymphoma assay and mouse micronucleus test. Not mutagenic in bacterial cells and other mammalian cell tests.

Section 12 - Ecological Information

No environmental data for the mixture or formulation. The environmental information for ingredient(s) or related material(s) are presented.

Ecotoxicity Data:

Gemcitabine

Rainbow trout 96-hour median lethal concentration: > 1043 mg/L

Fathead minnow 96-hour median lethal concentration: > 1014 mg/L

Daphnia magna 48-hour median effective concentration: > 999 mg/L

Green algae (*S. capricornutum*) median effective concentration: 5.4 mg/L (average specific growth rate)

Microorganisms

fungus (*Chaetomium globosum*): MIC > 1000 mg/L

mold (*Aspergillus flavus*): MIC > 1000 mg/L
soil bacteria (*Comamonas acidovorans*): MIC > 1000 mg/L
N-fixing bacteria (*Azotobacter chroococcum*): MIC > 1000 mg/L
blue-green algae (*Nostoc sp.*): MIC 800 mg/L

Environmental Fate:

Gemcitabine hydrochloride
Dissociation constant (pKa): 3.58
Kow: 0.053, 0.053, 0.052 (pH 5, 7, 9)
Solubility (g/L): 16.0, 15.3, 15.8 (pH 5, 7, 9)
Light absorption (nm): 268 - 269
Hydrolysis: no significant hydrolysis
Aerobic biodegradation half-life: 30% in 28 days

Environmental Summary:

Gemcitabine - Practically non-toxic to fish and microorganisms and moderately toxic to green algae. Low potential to bioaccumulate in aquatic organisms. Expected to be persistent in the environment based on slow rates of hydrolysis and biodegradation.

Lilly Aquatic Exposure Guideline (LAEG):

Gemcitabine hydrochloride
LAEG for Drinking Water: 0.045 micrograms/L
LAEG for Chronic Exposure: 1.0 micrograms/L
LAEG for Acute Exposure of Aquatic Organisms: 5400 micrograms/L

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.

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

Gemcitabine hydrochloride

TSCA - No

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

EU Regulations

EC Classification

Contains gemcitabine hydrochloride (C = 51 to 53%)

Xn (Harmful)

Xi (Irritant)

Reproductive Category 3

Mutagen Category 2

Risk Phrases

R 21 - Harmful in contact with skin.

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 46 - May cause heritable genetic damage.

Safety Phrases

S 25 - Avoid contact with eyes.

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

S 36/37 - Wear suitable protective clothing and gloves.

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

Section 16 - Other Information

MSDS Sections Revised: Section 2.

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)