



# Gemcitabine Hydrochloride for Injection

Eli Lilly and Company  
Material Safety Data Sheet

Effective Date: 11-Jun-1999

## Section 1 - Chemical Product and Company

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

**Emergency Phone:**  
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 Hydrochloride; Gemcitabine HCl; Gemcitabine; 264368 Formulation; 188011 Hydrochloride Formulation

**Tradename(s):** Gemzar; Gemcin; Gemtro

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

See attached glossary for abbreviations.

## Section 2 - Composition / Information on Ingredients

<u>Ingredient</u>	<u>CAS</u>	<u>Concentration %</u>
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 - PEL and TLV not established. LEG 0.2 micrograms/m<sup>3</sup> TWA for 12 hours, 2.4 micrograms/m<sup>3</sup> TWA for 30 minutes STEG.

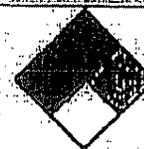
## Section 3 - Hazards Identification

**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.

**Potential Signs and Symptoms of Occupational Exposure:** 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:** 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 (HEPA) filters. 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.

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

See Section 8 for appropriate personal protective equipment.

## Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guidelines.

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 Directive Pub 8-1.1 - Guidelines for Cytotoxic (Antineoplastic) Drugs, 1986. This directive 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.

**Other Handling 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

**Boiling Point:** NA  
**Melting Point:** NAIF  
**Specific Gravity:** NAIF  
**pH:** Acidic  
**Evaporation Rate:** NAIF  
**Water Solubility:** Soluble  
**Vapor Density:** NAIF  
**Vapor Pressure:** NAIF

## 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

### Animal Toxicity Data Single Exposure

Data for Gemcitabine Hydrochloride for Injection and the active ingredient, gemcitabine hydrochloride, are presented as indicated.

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

**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:** Gemcitabine hydrochloride - No applicable information found.

**Intravenous:** Gemcitabine hydrochloride - Rat, median lethal dose 236 mg/kg, weight loss, reduced activity, drooping eyelids, hair loss, swollen face, eyes pale in color, emaciation, changes in stool.

**Skin Contact:** Gemcitabine Hydrochloride for Injection - Rabbit, irritant

**Eye Contact:** Gemcitabine hydrochloride - Rabbit, irritant

### Animal Toxicity Data Repeat Exposure

Data for the active ingredient, gemcitabine hydrochloride, are reported.

**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 cell tests and other mammalian cell tests.

## Section 12 - Ecological Information

### 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

Log 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 (days): no significant degradation

**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

Interim LAEG for Drinking Water: 0.0064 micrograms/L

Interim LAEG for Chronic Exposure: 1.3 micrograms/L

Interim LAEG for Acute Exposure of Aquatic Organisms: 6100 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:

TSCA - No

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

### EC Classification and Risk and Safety Phrases:

EC Classification:

Contains gemcitabine hydrochloride (C = 51 - 53%)

Xn (Harmful)

Xi (Irritant)

Reproductive Category 3

Mutagen Category 3

### Risk Phrases:

R 21 - Harmful in contact with skin.

R 36/38 - Irritating to eyes and skin.

R 40 - Possible risks of irreversible effects.

R 62 - Possible risk of impaired fertility.

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

### 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 12.

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

Environmental Science and Hazard Communication

317-277-4259

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)  
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  
LEG = Lilly Exposure Guideline  
LEL = Lower Explosive Limit  
MSDS = Material Safety Data Sheet  
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)