

CONTROL OF SUBSTANCES HAZARDOUS TO HEALTH (COSHH) SHEET

SECTION 1 – PRODUCT

PRODUCT NAME:

Gemcitabine Injection, 100 mg/mL

CHEMICAL NAME:

Cytidine, 2'-deoxy-2',2'-difluoro-, monohydrochloride

CHEMICAL NAME 2:

2'-Deoxy-2',2'-difluorocytidine monohydrochloride (beta-isomer)

SYNONYM:

Gemcitabine HCl formulation; Gemcitabine RTU

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

ACTIVE:

Gemcitabine Hydrochloride.

INACTIVE:

PEG-300 (Macrogol), Propylene Glycol, Sodium Hydroxide, Hydrochloric acid, Dehydrated Alcohol and Nitrogen

SECTION 3 - HAZARDS IDENTIFICATION

APPEARANCE:

Clear, colourless to pale yellow solution.

PHYSICAL STATE:

Liquid.

ODOR:

Odorless.

PRIMARY PHYSICAL AND HEALTH HAZARDS:

Skin permeable mutagen irritant (eyes, skin), reproductive and blood effects.

CAUTION STATEMENT:

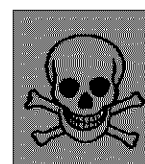
Gemcitabine Injection contains Gemcitabine Hydrochloride which may enter the body through the skin, alters genetic material, and may be irritating to the eyes and skin. Effects of exposure may include decreased fertility, fetal changes, and decreased blood cell counts.

ROUTES OF ENTRY:

Inhalation and skin absorption.

EFFECTS OF OVEREXPOSURE:

Based on animal data, Gemcitabine 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.



GEMCITABINE FOR INJECTION 100 MG/ML

MEDICAL CONDITIONS GENERALLY AGGRAVATED BY EXPOSURE:

None known.

CARCINOGENICITY:

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

SECTION 4 – EMERGENCY & 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

Keep out of the reach and sight of children.

This medicinal product does not require any specific storage condition.

It is recommended that the vial should remain in the carton until the time of use.

SECTION 8 – EXPOSURE CONTROLS/PERSONAL PROTECTION

EXPOSURE GUIDELINES:

Gemcitabine hydrochloride - LEG 0.3 micrograms/m³ TWA for 8 hours, LEG 0.2 micrograms/m³ TWA for 12 hours. Excursion Limit 2.4 micrograms/m³ for no more than a total of 30 minutes.

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

BOILING POINT:

No applicable information found.

MELTING POINT:

Not applicable.

DENSITY:

Not applicable.

pH::

7.0 to 8.0

EVAPORATION RATE:

No applicable information found.

WATER SOLUBILITY:

Miscible with water.

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 – TOXICOLOGY 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 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 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 - ENVIRONMENTAL IMPACT 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

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.

SECTION 13 – TRANSPORTATION INFORMATION**DOT:**

Not Regulated.

ICAO/IATA:

Not Regulated.

IMO:

Not Regulated.

SECTION 14 – DISPOSAL INFORMATION**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 15 – OTHER DATA

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Firm shall not be held liable for any damage resulting from handling or from contact with the above product.

SECTION 16 – DISCLAIMER

The information in this document is believed to be correct as of the date issued. HOWEVER, NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR ANY OTHER WARRANTY IS EXPRESSED OR IS TO BE IMPLIED REGARDING THE ACCURACY OR COMPLETENESS OF THIS INFORMATION, THE RESULTS TO BE OBTAINED FROM THE USE OF THIS INFORMATION OR THE PRODUCT, THE SAFETY OF THIS PRODUCT, OR THE HAZARDS RELATED TO ITS USE. This information and product are furnished on the condition that the person receiving them shall make his own determination as to the suitability of the product for his particular purpose and on the condition that he assume the risk of his use thereof.

GLOSSARY:

ACGIH = American Conference of Governmental Industrial Hygienists

DOT = Department of Transportation

HEPA = High Efficiency Particulate Air (Filter)

IARC = International Agency for Research on Cancer

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

IMO = International Maritime Organization

Kow = Octanol/Water Partition Coefficient

LEL = Lower Explosive Limit

MSDS = Material Safety Data Sheet

NA = Not Applicable

NTP = National Toxicology Program

OSHA = Occupational Safety and Health Administration

TWA = Time Weighted Average/8 Hours Unless Otherwise Noted

UEL = Upper Explosive Limit

RTU = Ready to use