



MATERIAL SAFETY DATA SHEET

Revision date: 20-Jun-2011

Version: 1.0

Page 1 of 9

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161
Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Gemcitabine Hydrochloride for Injection

| | |
|------------------|---|
| Trade Name: | Not applicable |
| Chemical Family: | Mixture |
| Intended Use: | Pharmaceutical product used as Antineoplastic |

2. HAZARDS IDENTIFICATION

Appearance: White to off-white Lyophilized powder
Signal Word: DANGER

Statement of Hazard: May be harmful if swallowed.
Causes eye irritation.
Causes skin irritation.
May cause genetic defects.
May damage fertility or the unborn child.

Additional Hazard Information:

| | |
|-------------|--|
| Short Term: | May be absorbed through the skin and cause systemic effects. |
| Long Term: | Repeat-dose studies in animals have shown a potential to cause adverse effects on reproductive system and blood and blood forming organs. Animal studies have shown a potential to cause adverse effects on the fetus. |

Known Clinical Effects: Adverse effects associated with therapeutic use include decreased blood cell count, nausea, vomiting, swelling, skin rash, liver enzyme changes, flu-like syndrome

| | |
|--------------------------|---|
| EU Indication of danger: | Harmful Irritant Toxic to Reproduction: Category 2 Mutagenic: Category 2 |
|--------------------------|---|

EU Hazard Symbols:



EU Risk Phrases:

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 2 of 9
Version: 1.0

2. HAZARDS IDENTIFICATION

Australian Hazard Classification (NOHSC):

R22 - Harmful if swallowed.
R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R36/38 - Irritating to eyes and skin.
Hazardous Substance. Non-Dangerous Goods.

Note:

This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

| Ingredient | CAS Number | EU EINECS/ELINCS List | EU Classification | % |
|---------------------------|-------------|-----------------------|--|-------|
| Gemcitabine hydrochloride | 122111-03-9 | Not Listed | Xn,R22; Xi, R36/38; Repr. Cat. 2,R60-61; Mut. Cat. 2,R46 | 51-53 |
| Sodium hydroxide | 1310-73-2 | 215-185-5 | C;R35 | ** |
| Hydrochloric Acid | 7647-01-0 | 231-595-7 | C;R35 T;R23 | ** |

| Ingredient | CAS Number | EU EINECS/ELINCS List | EU Classification | % |
|----------------|------------|-----------------------|-------------------|---|
| Mannitol | 69-65-8 | 200-711-8 | Not Listed | * |
| Sodium acetate | 127-09-3 | 204-823-8 | Not Listed | * |

Additional Information:

* Proprietary

** to adjust pH

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Eye Contact:

Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact:

Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion:

Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation:

Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Symptoms and Effects of Exposure:

For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 3 of 9
Version: 1.0

5. FIRE FIGHTING MEASURES

| | |
|--------------------------------|---|
| Extinguishing Media: | Use carbon dioxide, dry chemical, or water spray. |
| Hazardous Combustion Products: | Formation of toxic gases is possible during heating or fire. |
| Fire Fighting Procedures: | During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus. |
| Fire / Explosion Hazards: | Fine particles (such as dust and mists) may fuel fires/explosions. |

6. ACCIDENTAL RELEASE MEASURES

| | |
|--|--|
| Health and Safety Precautions: | Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure. |
| Measures for Cleaning / Collecting: | Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly. |
| Measures for Environmental Protections: | Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release. |
| Additional Consideration for Large Spills: | Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel. |

7. HANDLING AND STORAGE

| | |
|---------------------|---|
| General Handling: | Restrict access to work area. Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. |
| Storage Conditions: | Store as directed by product packaging. |

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Sodium hydroxide

| | |
|--------------------------------|---------------------|
| ACGIH Ceiling Threshold Limit: | 2 mg/m ³ |
| Australia PEAK | 2 mg/m ³ |
| Austria OEL - MAKs | Listed |
| Bulgaria OEL - TWA | Listed |
| Czech Republic OEL - TWA | Listed |
| Estonia OEL - TWA | Listed |
| France OEL - TWA | Listed |
| Greece OEL - TWA | Listed |
| Hungary OEL - TWA | Listed |
| Japan - OELs - Ceilings | 2 mg/m ³ |
| Latvia OEL - TWA | Listed |
| OSHA - Final PELs - TWAs: | 2 mg/m ³ |
| Poland OEL - TWA | Listed |

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 4 of 9
Version: 1.0

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

| | |
|--------------------|--------|
| Slovenia OEL - TWA | Listed |
| Sweden OEL - TWAs | Listed |

Hydrochloric Acid

| | |
|--------------------------------|---------------------------|
| ACGIH Ceiling Threshold Limit: | 2 ppm |
| Australia PEAK | 5 ppm |
| | 7.5 mg/m ³ |
| Austria OEL - MAKs | Listed |
| Belgium OEL - TWA | Listed |
| Bulgaria OEL - TWA | Listed |
| Cyprus OEL - TWA | Listed |
| Czech Republic OEL - TWA | Listed |
| Estonia OEL - TWA | Listed |
| Germany - TRGS 900 - TWAs | 2 ppm |
| | 3 mg/m ³ |
| Germany (DFG) - MAK | 2 ppm MAK |
| | 3.0 mg/m ³ MAK |
| Greece OEL - TWA | Listed |
| Hungary OEL - TWA | Listed |
| Ireland OEL - TWAs | Listed |
| Italy OEL - TWA | Listed |
| Japan - OELs - Ceilings | 5 ppm |
| | 7.5 mg/m ³ |
| Latvia OEL - TWA | Listed |
| Lithuania OEL - TWA | Listed |
| Luxembourg OEL - TWA | Listed |
| Malta OEL - TWA | Listed |
| Netherlands OEL - TWA | Listed |
| Poland OEL - TWA | Listed |
| Romania OEL - TWA | Listed |
| Slovenia OEL - TWA | Listed |
| Spain OEL - TWA | Listed |

Gemcitabine hydrochloride

| | |
|--|--|
| Pfizer Occupational Exposure Band (OEB): | OEB 5 - Skin (control exposure to <1ug/m ³ , provide additional precautions to protect from skin contact) |
|--|--|

Engineering Controls:

Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Environmental Exposure Controls:

Refer to specific Member State legislation for requirements under Community environmental legislation.

Personal Protective Equipment:

Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

| | |
|---------------|--|
| Hands: | Impervious, disposable gloves (double suggested) are recommended if skin contact with drug product is possible and for bulk processing operations. |
|---------------|--|

| | |
|--------------|--|
| Eyes: | Wear safety glasses or goggles if eye contact is possible. |
|--------------|--|

| | |
|--------------|--|
| Skin: | Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. |
|--------------|--|

| | |
|--------------------------------|--|
| Respiratory protection: | If airborne exposures are within or exceed the Occupational Exposure Band (OEB) range, wear an appropriate respirator with a protection factor sufficient to control exposures to the bottom of the OEB range. |
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MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 5 of 9
Version: 1.0

9. PHYSICAL AND CHEMICAL PROPERTIES

| | | | |
|--|------------------------|-------------------|--------------------|
| Physical State: | Lyophilized powder | Color: | White to off-white |
| Molecular Formula: | Mixture | Molecular Weight: | Mixture |
| Water solubility: | 15.3 g/L (gemcitabine) | | |
| Partition Coefficient (Calculated - Log Pow/Log Kow): | 1.27 (gemcitabine) | | |

10. STABILITY AND REACTIVITY

| | |
|-------------------------|--|
| Chemical Stability: | Stable under normal conditions of use. |
| Conditions to Avoid: | Fine particles (such as dust and mists) may fuel fires/explosions. |
| Incompatible Materials: | As a precautionary measure, keep away from strong oxidizers |

11. TOXICOLOGICAL INFORMATION

| | |
|----------------------|---|
| General Information: | The information included in this section describes the potential hazards of the individual ingredients. |
|----------------------|---|

Acute Toxicity: (Species, Route, End Point, Dose)

Mannitol

| | | | |
|-------|------|-------|-------------|
| Rat | Oral | LD 50 | 13500 mg/kg |
| Mouse | Oral | LD 50 | 22 g/kg |

Sodium hydroxide

| | | | |
|-------|----|------|----------|
| Mouse | IP | LD50 | 40 mg/kg |
|-------|----|------|----------|

Gemcitabine hydrochloride

| | | | |
|--------|--------|---------------------|--------------|
| Mouse | Oral | Minimum Lethal Dose | 333 mg/kg |
| Rat | Oral | LD50 | > 500 mg/kg |
| Rabbit | Dermal | LD50 | > 1000 mg/kg |

| | |
|--------------------------|--|
| Acute Toxicity Comments: | A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test. |
|--------------------------|--|

Irritation / Sensitization: (Study Type, Species, Severity)

Sodium hydroxide

| | | |
|-----------------|--------|--------|
| Eye Irritation | Rabbit | Severe |
| Skin Irritation | Rabbit | Severe |

Gemcitabine hydrochloride

| | | |
|-----------------|--------|----------|
| Skin Irritation | Rabbit | Irritant |
| Eye Irritation | Rabbit | Irritant |

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Gemcitabine hydrochloride

| | | | | | |
|------------|-------|--------------------|-----------------|-------|--|
| 6 Month(s) | Dog | No route specified | 0.04 mg/kg/day | NOAEL | Blood, Erythroid cells, Lymphoid tissue, Immune system |
| 6 Month(s) | Mouse | No route specified | 0.006 mg/kg/day | LOAEL | Erythroid cells, Male reproductive system, Spleen |

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 6 of 9
Version: 1.0

11. TOXICOLOGICAL INFORMATION

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Gemcitabine hydrochloride

| | | | | | |
|--|-------|-----------------|----------------|-------|--|
| Reproductive & Fertility | Mouse | Intraperitoneal | 0.05 mg/kg/day | NOAEL | Fertility |
| Fertility and Embryonic Development Toxicity | Mouse | Intravenous | 0.25 mg/kg/day | LOAEL | Fetotoxicity, Embryotoxicity, Maternal |

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Gemcitabine hydrochloride

| | | |
|---|------------------------------------|----------|
| <i>In Vivo</i> Micronucleus | Mouse | Positive |
| <i>In Vitro</i> Mammalian Cell Mutagenicity | Mouse Lymphoma | Positive |
| Bacterial Mutagenicity (Ames) | <i>Salmonella</i> , <i>E. coli</i> | Negative |
| <i>In Vivo</i> Sister Chromatid Exchange | | Negative |
| <i>In Vitro</i> Chromosome Aberration | | Negative |

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Hydrochloric Acid

IARC: Group 3

12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

Partition Coefficient 1.27 (gemcitabine)
(Calculated - Log Pow/Log Kow):

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Gemcitabine hydrochloride

| | | | |
|---|------|----------|-------------|
| <i>Oncorhynchus mykiss</i> (Rainbow Trout) | LC50 | 96 Hours | > 1043 mg/L |
| <i>Pimephales promelas</i> (Fathead Minnow) | LC50 | 96 Hours | > 1014 mg/L |
| <i>Daphnia Magna</i> (Water Flea) | EC50 | 48 Hours | > 999 mg/L |
| <i>Selenastrum capricornutum</i> (Green Alga) | EC50 | 5.4 | mg/L |

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Gemcitabine hydrochloride

| | | |
|--|-----|-------------|
| <i>Nostoc</i> sp. (Freshwater Cyanobacteria) | MIC | 800 mg/L |
| <i>Aspergillus niger</i> (Fungus) | MIC | > 1000 mg/L |

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods:

Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 7 of 9
Version: 1.0

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

EU Symbol: T
EU Indication of danger: Harmful
Irritant
Toxic to Reproduction: Category 2
Mutagenic: Category 2

EU Risk Phrases:

R22 - Harmful if swallowed.
R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R36/38 - Irritating to eyes and skin.

EU Safety Phrases:

S22 - Do not breathe dust.
S53 - Avoid exposure - obtain special instructions before use.
S36/37 - Wear suitable protective clothing and gloves.

OSHA Label:

DANGER
May be harmful if swallowed.
Causes eye irritation.
Causes skin irritation.
May cause genetic defects.
May damage fertility or the unborn child.

Canada - WHMIS: Classifications

WHMIS hazard class:

Class D, Division 2, Subdivision A



Sodium hydroxide

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 8 of 9
Version: 1.0

15. REGULATORY INFORMATION

| | |
|---|------------------|
| CERCLA/SARA Hazardous Substances and their Reportable Quantities: | 1000 lb final RQ |
| Inventory - United States TSCA - Sect. 8(b) | 454 kg final RQ |
| Australia (AICS): | Listed |
| Standard for the Uniform Scheduling for Drugs and Poisons: | Listed |
| EU EINECS/ELINCS List | Schedule 5 |
| | Schedule 6 |
| | 215-185-5 |

Hydrochloric Acid

| | |
|--|--|
| CERCLA/SARA 313 Emission reporting | 1.0% de minimis concentration acid aerosols including mists, vapors, gas, fog, and other airborne forms of any particle size |
| CERCLA/SARA Hazardous Substances and their Reportable Quantities: | 2270 kg final RQ |
| CERCLA/SARA - Section 302 Extremely Hazardous TPQs | 5000 lb final RQ |
| CERCLA/SARA - Section 302 Extremely Hazardous Substances EPCRA RQs | 500 lb TPQ gas only |
| Inventory - United States TSCA - Sect. 8(b) | 5000 lb |
| Australia (AICS): | Listed |
| Standard for the Uniform Scheduling for Drugs and Poisons: | Listed |
| EU EINECS/ELINCS List | Schedule 5 |
| | Schedule 6 |
| | 231-595-7 |

Mannitol

| | |
|---|-----------|
| Inventory - United States TSCA - Sect. 8(b) | Listed |
| Australia (AICS): | Listed |
| REACH - Annex IV - Exemptions from the obligations of Register: | Present |
| EU EINECS/ELINCS List | 200-711-8 |

Sodium acetate

| | |
|---|-----------|
| Inventory - United States TSCA - Sect. 8(b) | Listed |
| Australia (AICS): | Listed |
| EU EINECS/ELINCS List | 204-823-8 |

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R23 - Toxic by inhalation.
R35 - Causes severe burns.
R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R36/38 - Irritating to eyes and skin.

Data Sources: Publicly available toxicity information. Safety data sheets for individual ingredients.

Prepared by: Product Stewardship Hazard Communications
Pfizer Global Environment, Health, and Safety Operations

MATERIAL SAFETY DATA SHEET

Material Name: Gemcitabine Hydrochloride for Injection
Revision date: 20-Jun-2011

Page 9 of 9
Version: 1.0

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End of Safety Data Sheet