



## MATERIAL SAFETY DATA SHEET

### Clolar® for Intravenous Infusion

#### 1. PRODUCT AND COMPANY IDENTIFICATION

**Product Name:** Clolar® for Intravenous Infusion

**Synonym(s):** Clofarabine; Evoltra®

**Product Use:** Clolar® is indicated for the treatment of pediatric patients 1 to 21 years old with relapsed or refractory acute lymphoblastic leukemia after at least two prior regimens.

**Description:** Clolar® contains clofarabine, a purine nucleoside anti-metabolite, formulated in unbuffered normal saline (comprised of Water for Injection, USP, and sodium chloride, USP).

**Corporate Headquarters**

**Genzyme Corporation**

500 Kendall Street  
Cambridge, MA 02142  
USA

**Phone:** +1 617-252-7500

**Manufactured For**

**Genzyme Corporation**

4545 Horizon Hill Blvd  
San Antonio, TX 78229  
USA

**Phone:** +1 210-949-8200

**Emergency Telephone Numbers**

**Genzyme (U.S.):** +1 617-562-4555

**CHEMTREC (U.S.):** 1-800-424-9300

**CHEMTREC (Outside U.S.):** +1 703-527-3887

#### 2. HAZARDS IDENTIFICATION

**Precautionary Statements:**

The chemical, physical and toxicological properties of this preparation have not been thoroughly characterized. CAUTION! Clolar® contains a small concentration of clofarabine which is cytotoxic to rapidly proliferating cells, genotoxic, and a potential teratogen. Due to the dilution of clofarabine (0.1%) in Clolar®, the risk of clofarabine exposure and toxicity is greatly reduced. May be harmful if swallowed. Avoid contact with eyes and skin. Do not ingest or inhale. Preparation appearance: clear, colorless liquid.

**Routes of Exposure:**

Occupational exposure routes may include eye and skin contact.

**Potential Health Effects:**

<b>Inhalation</b>	Inhalation is not an expected route of exposure during normal use.
<b>Eye</b>	Eye exposure is expected to be nonirritating, based on animal studies.
<b>Skin</b>	Skin exposure is expected to be nonirritating, based on animal studies.
<b>Ingestion</b>	Ingestion may cause effects similar to those known to occur by the IV route, including vomiting, nausea, and diarrhea; and blood system effects such as decreased red blood cells, decreased white blood cells, and low blood platelet levels.
<b>Chronic Effects</b>	Clofarabine is genotoxic. Prolonged or repeated exposure may cause harmful or toxic target organ effects.
<b>Medical Conditions Aggravated By Exposure</b>	Clofarabine is a potential teratogen. Take precautionary measures when working with this preparation if pregnant or nursing.
<b>Target Organs</b>	Lymphoid tissue, bone marrow, GI tract, and testes.

**Regulatory Status:**

This preparation is not classified as hazardous under U.S. OSHA 29 CFR 1910.1200; E.C. Directive 1999/45/EC; or U.N. GHS ST/SG/AC 10/30.

None of the components present in this preparation at concentrations equal to or greater than 0.1% are listed by IARC, NTP, OSHA or ACGIH as a carcinogen.



## MATERIAL SAFETY DATA SHEET

### Clolar® for Intravenous Infusion

#### 3. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredient Name	CAS #	EC #	% (wt/wt)
Water	7732-18-5	231-791-2	99
EC R-Phrases: None	EC Hazard Class: None		
Sodium chloride	7647-14-5	231-598-3	0.9
EC R-Phrases: None	EC Hazard Class: None		
Clofarabine [2-Chloro-9-(2'-deoxy-2'-fluoro-β-D-arabinofuranosyl)-9H-purin-6-amine]	123318-82-1	Not Assigned	0.1
EC R-Phrases: None	EC Hazard Class: None		

#### 4. FIRST AID MEASURES

**Inhalation:**

If inhaled, move from exposure area to fresh air. Seek immediate medical attention if breathing becomes difficult or if cough or other symptoms develop.

**Eye Contact:**

Immediately flush eyes with plenty of tepid water for 15 minutes while separating eyelids with fingers. Remove contact lenses if worn. Obtain medical attention if needed or if symptoms, such as redness or irritation persist.

**Skin Contact:**

In case of contact, immediately flush skin with copious amounts of cool water and remove contaminated clothing. Obtain medical attention if needed or if irritation or other symptoms develop.

**Ingestion:**

In case of ingestion, contact a poison control center and seek immediate medical attention.

#### 5. FIRE FIGHTING MEASURES

**Flammable Properties:**

Dilute aqueous solution not considered a fire hazard.

**Suitable Extinguishing Media:**

Use extinguishing media suitable for surrounding fire, such as carbon dioxide, chemical foam, dry chemical or water spray.

**Unsuitable Extinguishing Media:**

Unknown.

**Specific Hazards Arising from the Chemical:**

None known.

**Standard Protective Equipment and Precautions for Firefighters:**

Firefighters should wear NIOSH-approved or equivalent Self-Contained Breathing Apparatus and full protective gear.



## MATERIAL SAFETY DATA SHEET

### Clolar® for Intravenous Infusion

#### 6. ACCIDENTAL RELEASE MEASURES

**Personal Precautions:**

Wear Personal Protective Equipment (PPE) as indicated in Section 8. Avoid physical contact with material and avoid aerosol inhalation.

**Environmental Precautions:**

No information available.

**Methods and Materials for Containment and Clean-Up:**

Absorb spill with inert material/sorbent. Decontaminate the spill site following standard procedures. Dispose of materials in accordance with all applicable federal, state, local and provincial environmental regulations, per Section 13.

#### 7. HANDLING AND STORAGE

**Handling:**

Follow good laboratory hygiene practices for the handling and use of cytotoxic drugs. See Section 8, Engineering Controls. Wash hands thoroughly after handling.

**Storage:**

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

#### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Exposure Guidelines:**

There are no ACGIH, NIOSH, OSHA or country-specific occupational exposure limits currently established for components present in this preparation at concentrations equal to or greater than 1% (0.1% if carcinogen).

The Genzyme occupational exposure limit (OEL) for clofarabine is 0.2 µg/m<sup>3</sup> as an 8-hour TWA. The Genzyme OEL is based upon the best scientific information available at this time.

**Engineering Controls:**

Follow cytotoxic drug handling procedures.

Facilities storing or using this material should be equipped with an eyewash fountain and a safety shower.

**Personal Protective Equipment (PPE):**

<b>Respiratory</b>	Respiratory protection should not be necessary under normal work conditions and if appropriate engineering controls are in place.
<b>Eye/Face</b>	Wear appropriate protective chemical safety glasses.
<b>Skin</b>	Wear lab coat or other protective garments. Remove contaminated clothing promptly.
<b>Gloves</b>	Wear chemical resistant protective gloves. Change gloves regularly or immediately if they are contaminated, torn or punctured.
<b>General</b>	Follow company-specific safety procedures.

#### 9. PHYSICAL AND CHEMICAL PROPERTIES

<b>Appearance:</b>	Clear, colorless liquid	<b>pH:</b>	4.5 - 7.5
<b>Molecular Weight:</b>	303.68 (Clofarabine)	<b>Solubility:</b>	Water-soluble
<b>Odor:</b>	Unknown	<b>Vapor Pressure:</b>	Not available
<b>Specific Gravity:</b>	1.006		



## MATERIAL SAFETY DATA SHEET

### Clolar® for Intravenous Infusion

<b>Boiling Point:</b>	Not available	<b>Partition Coefficient (n-octanol/water):</b>	Not available
<b>Melting Point:</b>	Not applicable	<b>Vapor Density:</b>	Not available
<b>Freezing Point:</b>	Not available		
<b>Molecular Formula:</b>	C <sub>10</sub> H <sub>11</sub> ClF <sub>5</sub> N <sub>5</sub> O <sub>3</sub> (Clofarabine)		
<b>Flammability/Explosivity Limits in Air, Lower:</b>	Not available		
<b>Flammability/Explosivity Limits in Air, Upper:</b>	Not available		
<b>Auto-Ignition Temperature:</b>	Not available		
<b>Flash Point:</b>	Not available		

### 10. STABILITY AND REACTIVITY

**Chemical Stability:**

Stable under ordinary conditions of use and storage. See Section 7.

**Incompatible Materials:**

Unknown.

**Hazardous Decomposition Products:**

None expected under normal conditions of use.

**Possibility of Hazardous Reactions:**

Hazardous polymerization will not occur.

### 11. TOXICOLOGICAL INFORMATION

**Acute Effects:**

Clofarabine was nonirritating to the skin and eyes in rabbit models.

**Lethal Dose Finding Studies in Animals for Clofarabine:**

LD<sub>10</sub> (mouse): 75 mg/kg/day for 7 days by intraperitoneal injection.

LD (rat): 50 mg/kg/day for 5 days by intravenous injection.

LD (dog) 3.0 mg/kg/day for 5 days by intravenous injection.

Single daily dose oral toxicity (rats), 21 day study: LLD 30 mg/kg/day with LOAEL of 3 mg/kg/day.

**Chronic Effects:**

Clofarabine can cause myelosuppression.

**Carcinogenicity:**

Clofarabine has not been tested for carcinogenic potential.

**Mutagenicity:**

Negative in the bacterial gene mutation assay (Ames test); clastogenic activity in the *in vitro* mammalian cell chromosome aberration assay in CHO cells and in the *in vivo* rat micronucleus assay.

**Teratogenicity:**

Clofarabine was embryotoxic and teratogenic in rats and rabbits.

**Reproductive Effects:**

Studies in mice, rats, and dogs have demonstrated dose-related adverse effects on male reproductive organs.

### 12. ECOLOGICAL INFORMATION

**Ecotoxicity:**

No information available for product.



## MATERIAL SAFETY DATA SHEET

### Clolar® for Intravenous Infusion

**Persistence and Degradability:**

No data available.

**Bioaccumulative Potential:**

No data available.

**Mobility in Environmental Media:**

No data available.

### 13. DISPOSAL CONSIDERATIONS

**Methods of Disposal:**

Dispose of unused product, spilled material and waste in accordance with all applicable federal, state, local and provincial environmental and hazardous waste regulations. Unused, expired, and waste product, as well as contaminated waste should be handled as hazardous, cytotoxic waste.

### 14. TRANSPORT INFORMATION

**Basic Shipping Description:**

Not classified as dangerous goods. Not regulated per IATA and DOT regulations.

### 15. REGULATORY INFORMATION

**US Federal Regulations:**

This pharmaceutical preparation is regulated by the U.S. FDA.

**International Regulations:**

This preparation is intended for use as a medicinal product. If approved for use in the EU, it is regulated under the Medicinal Products Directive (2001/83/EC) and is exempt from classification under the Dangerous Substances Directive (67/548/EC).

**Canadian Hazardous Products:**

WHMIS Status          Exempt

**European Communities Dangerous Substances/Preparations:**

EC Hazard Class          Exempt

Risk Phrases None

Safety Phrases None

### 16. OTHER INFORMATION

**Further Information:**

This MSDS has been prepared in accordance with the ANSI Z400.1 format. Every effort has been made to adhere to the hazard criteria and content requirements of the U.S. OSHA Hazard Communication Standard, Canadian Controlled Products Regulations, UK Chemical Hazard Information and Packaging Regulations, European Communities REACH Regulation, and UN Globally Harmonized System of Classification and Labelling of Chemicals.



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**Disclaimer:**

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