

SAFETY DATA SHEET

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Trade name or designation of the mixture	Pemetrexed Disodium Heptahydrate for Injection
Registration number	-
Synonyms	L-Glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo-1H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]-, disodium salt, heptahydrate
Item Code	VL7623, VL7640

1.2. Relevant identified uses of the substance or mixture and uses advised against

Identified uses	Pharmaceutical
Uses advised against	None known.

1.3. Details of the supplier of the safety data sheet

Supplier

Company name	Eli Lilly and Company
Address	Lilly Corporate Center Indianapolis, IN 46285 United States
Division	
Telephone	Phone: +1-317-276-2000
e-mail	lilly_msds@lilly.com

1.4. Emergency telephone number	CHEMTREC: +1-703-527-3887
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SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

The substance has been assessed and/or tested for its physical, health and environmental hazards and the following classification applies.

Classification according to Directive 67/548/EEC or 1999/45/EC as amended

Classification	Muta. Cat. 3;R68, Repr. Cat. 1;R60-61, Xi;R38
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Classification according to Regulation (EC) No 1272/2008 as amended

Health hazards

Skin corrosion/irritation	Category 2	H315 - Causes skin irritation.
Germ cell mutagenicity	Category 2	H341 - Suspected of causing genetic defects.
Reproductive toxicity	Category 1A	H360FD - May damage fertility. May damage the unborn child.
Specific target organ toxicity - repeated exposure	Category 1 (blood)	H372 - Causes damage to organs (Blood) through prolonged or repeated exposure.

2.2. Label elements

Label according to Regulation (EC) No. 1272/2008 as amended

Contains:	Pemetrexed Disodium Heptahydrate
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Hazard pictograms



Signal word	Danger
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Hazard statements

H315	Causes skin irritation.
H341	Suspected of causing genetic defects.
H360FD	May damage fertility. May damage the unborn child.
H372	Causes damage to organs (Blood) through prolonged or repeated exposure.

Precautionary statements

Prevention

P201	Obtain special instructions before use.
P202	Do not handle until all safety precautions have been read and understood.
P264	Wash thoroughly after handling.
P281	Use personal protective equipment as required.

Response

P308 + P313	IF exposed or concerned: Get medical advice/attention.
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Storage

P405	Store locked up.
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Disposal

P501	Dispose of contents/container in accordance with local/regional/national/international regulations.
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Supplemental label information

None.

2.3. Other hazards

None known.

SECTION 3: Composition/information on ingredients

3.2. Mixtures

General information

Chemical name	%	CAS-No. / EC No.	REACH Registration No.	INDEX No.	Notes
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Pemetrexed Disodium Heptahydrate	50	357166-29-1	-	-	
Classification:	DSD:	Muta. Cat. 3;R68, Repr. Cat. 1;R60-61, Xi;R38			
	CLP:	Skin Irrit. 2;H315, Muta. 2;H341, Repr. 1A;H360FD, STOT RE 1;H372			

CLP: Regulation No. 1272/2008.

DSD: Directive 67/548/EEC.

Composition comments

The full text for all R- and H-phrases is displayed in section 16.
Remaining components of this product are non-hazardous and/or are present at concentrations below reportable levels.

SECTION 4: First aid measures

General information

Not available.

4.1. Description of first aid measures

Inhalation	Remove to fresh air. If breathing stops, provide artificial respiration. Get medical attention immediately.
Skin contact	Wash off immediately with plenty of water. Continue to rinse for at least 15 minutes. Immediately take off all contaminated clothing. Get medical attention if irritation develops and persists. Wash contaminated clothing before reuse.
Eye contact	In case of eye contact, remove contact lens and rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Get medical attention.
Ingestion	If conscious, give the victim plenty of water to drink. Never give anything by mouth to a victim who is unconscious or is having convulsions. Call a physician immediately.

4.2. Most important symptoms and effects, both acute and delayed

Causes skin irritation. May cause redness and pain. Decreased fetal weight and viability have been reported in animal studies with pemetrexed disodium. The active ingredient, pemetrexed, is a folic acid antimetabolite, this class of compounds is known to cause developmental effects. Dilute solutions of pemetrexed disodium are not expected to be irritating to the eyes or skin. Effects of overexposure to pemetrexed disodium may include bone marrow suppression resulting in decreased blood cell counts, inflammation of mucous membranes, skin rash, fatigue, fetal effects, and reproductive tissue changes.

4.3. Indication of any immediate medical attention and special treatment needed

If overdose occurs, general supportive measures should be instituted as deemed necessary by the treating physician. Management of pemetrexed overdose should include consideration of the use of leucovorin or thymidine rescue.

SECTION 5: Firefighting measures

General fire hazards

Not available.

5.1. Extinguishing media

Suitable extinguishing media Carbon dioxide, dry chemical or water.

Unsuitable extinguishing media None known.

5.2. Special hazards arising from the substance or mixture Hazardous decomposition products formed under fire conditions.

5.3. Advice for firefighters

Special protective equipment for firefighters Wear self-contained breathing apparatus and protective clothing.

Special fire fighting procedures Not available.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

For non-emergency personnel Wear suitable protective clothing, gloves and eye/face protection. See Section 8 for personal protective equipment.

For emergency responders Not available.

6.2. Environmental precautions Avoid discharge into drains, water courses or onto the ground.

6.3. Methods and material for containment and cleaning up 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.

6.4. Reference to other sections Refer to Sections 8, 11, 12 and 13 for more information.

SECTION 7: Handling and storage

7.1. Precautions for safe handling Provide adequate ventilation. Avoid contact with eyes, skin, and clothing. Wash hands thoroughly after handling. See Section 8 for personal protective equipment.

7.2. Conditions for safe storage, including any incompatibilities Storage temperature: between 20 and 25 °C (68 to 77 °F). Excursions permitted from 15 to 30 °C (59 to 86 °F). [see USP]. Premetrexed is not light sensitive. Keep in original container.

7.3. Specific end use(s) Not available.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Recommended monitoring procedures Not available.

Occupational exposure limits

Lilly (LEG)

Components	Type	Value	Form
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)	Excursion Limit	3,6 ug/m3	30 minutes
	TWA (12hrs)	0,3 ug/m3	
	TWA (8hrs)	0,3 ug/m3	

Occupational exposure limits No exposure limits noted for ingredient(s).

Biological limit values No biological exposure limits noted for the ingredient(s).

Derived no-effect level (DNEL) Not available.

Predicted no effect concentrations (PNECs) Not available.

8.2. Exposure controls

Appropriate engineering controls	Extensive local exhaust, ventilated enclosure (HEPA-filtered balance enclosure, fume hood, or Class II or III vertical flow biosafety cabinet), or enclosed process equipment.
Individual protection measures, such as personal protective equipment	
General information	Not available.
Eye/face protection	Safety glasses with side-shields conforming to EN 166.
Skin protection	
- Hand protection	Chemical-resistant gloves and impermeable body covering to minimize skin contact.
- Other	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.
Respiratory protection	When the exposure guidelines may be exceeded, use an approved HEPA-filtered or supplied-air respirator. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).
Thermal hazards	Not available.
Hygiene measures	For appropriate handling precautions in specific laboratory, manufacturing, or clinical health care operations, consult with a health and safety or technical services representative. GENERAL: For all work environments, wear eye protection and ELIMINATE hand-to-eye contact. Avoid skin contact, wear gloves, and take other appropriate precautions.
	In production settings, airline-supplied, hood-type respirators are preferred. Shower and change clothing if skin contact occurs.
Environmental exposure controls	Not available.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Appearance

Physical state	Solid.
Form	Solid. (Lyophilised).
Colour	White.
Odour	Odourless.
Odour threshold	No data available.
pH	No data available.
Melting point/freezing point	No data available.
Initial boiling point and boiling range	No data available.
Flash point	Not applicable.
Evaporation rate	No data available.
Flammability (solid, gas)	No test data available.

Upper/lower flammability or explosive limits

Flammability limit - lower (%)	No data available.
Flammability limit - upper (%)	No data available.
Explosive limit - lower (%)	No data available.
Explosive limit – upper (%)	No data available.

Vapour pressure	No data available.
Vapour density	No data available.
Relative density	No data available.
Solubility(ies)	89,4 g/l , (pH 9), (as free acid) 101,5 g/l , (pH 7), (as free acid)
Partition coefficient (n-octanol/water)	< 1,000
Auto-ignition temperature	No data available.
Decomposition temperature	No data available.

Viscosity	Not applicable.
Explosive properties	Not explosive
Oxidizing properties	The substance or mixture is not classified as oxidizing.

9.2. Other information

Density	No data available.
Minimum ignition temperature	No data available.
Percent volatile	No data available.
VOC (Weight %)	No data available.

SECTION 10: Stability and reactivity

10.1. Reactivity	Not water reactive.
10.2. Chemical stability	Material is stable under normal conditions.
10.3. Possibility of hazardous reactions	Hazardous polymerisation does not occur.
10.4. Conditions to avoid	None known.
10.5. Incompatible materials	Strong oxidising agents.
10.6. Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.

SECTION 11: Toxicological information

General information	Not available.
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11.1. Information on toxicological effects

Components	Species	Test results
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)		
Acute		
<i>Dermal</i>		
LD	Rabbit	> 1000 mg/kg
<i>Oral</i>		
LD	Rat	> 500 mg/kg , (as free base)
<i>Other</i>		
LD50	Rat	> 1574 mg/kg , Intravenous (female), Convulsions. Mortality. 1332 mg/kg , Intravenous (male), Convulsions.
Skin corrosion/irritation	Rabbit: Irritating to skin.	
Serious eye damage/eye irritation	Rabbit: Mild eye irritation. (cleared within 7 days) Based on available data, the classification criteria are not met.	
Respiratory sensitisation	Due to lack of data the classification is not possible.	
Skin sensitisation	No test data available. Skin rash has been reported in patients not pretreated with a cortiosteroid (dexamethasone). Based on available data, the classification criteria are not met.	
Germ cell mutagenicity	Clastogenic in the in vivo micronucleus assay in the mouse. Results in genetic toxicity assays (in vitro): Negative	
Carcinogenicity	Not listed by IARC, NTP, ACGIH or OSHA. Due to lack of data the classification is not possible.	
Reproductive toxicity	Administration to pregnant mice resulted in decreased fetal weight, incomplete ossification of some skeletal structures, and cleft palate. Male reproductive toxicity characterized by reduced fertility, hypospermia, and testicular atrophy was observed when given to male mice.	
Specific target organ toxicity - single exposure	Due to lack of data the classification is not possible.	
Specific target organ toxicity - repeated exposure	Causes damage to organs (Blood) through prolonged or repeated exposure. Decreased testes weights with decreased sperm production and decreased red blood cells were reported in mice with intraperitoneal exposure for 6 weeks. Intravenous exposure in dogs for up to 6 months resulted in mortality, decreased white blood cell counts, mild anemia, and intestinal lesions.	
Aspiration hazard	Not applicable.	
Mixture versus substance information	No information available.	

Other information

Patients are instructed to take folic acid and vitamin B12 to reduce treatment related toxicity.

SECTION 12: Ecological information**12.1. Toxicity**

Components		Species	Test results
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)			
<i>Acute</i>			
	EC50	Algae (Pseudokirchnerella subcapitata)	63 mg/l, 72 h (average specific growth rate) (as free acid) 17 mg/l, 72 h (yield) (as free acid)
		Respiration inhibition of activated sludge	1000 mg/l, 3 h (highest concentration tested) (as free acid)
	NOEC	Respiration inhibition of activated sludge	> 1000 mg/l, 3 h (highest concentration tested) (as free acid)
<i>Chronic</i>			
	LOEC	Midge (Chironomus riparius)	> 100000 µg/l, 28 h (highest concentration tested)
	NOEC	Algae (Pseudokirchnerella subcapitata)	11 mg/l, 72 h (average specific growth rate) (as free acid) 4 mg/l, 72 h (yield) (as free acid)
		Midge (Chironomus riparius)	100000 µg/l, 28 h (highest concentration tested)
Aquatic			
<i>Acute</i>			
Crustacea	EC50	Daphnia magna	462 mg/l, 48 h (as free acid)
	NOEC	Daphnia magna	91,8 mg/l, 48 h (as free acid)
Fish	LC50	Rainbow trout,donaldson trout (Oncorhynchus mykiss)	> 1099,6 mg/l, 96 h (highest concentration tested) (as free acid)
<i>Chronic</i>			
Crustacea	EC50	Daphnia magna	1,8 mg/l, 21 d (reproduction)(as free acid)
	LOEC	Daphnia magna	2,1 mg/l, 21 d (as free acid)
	NOEC	Daphnia magna	1,2 mg/l, 21 d (as free acid)
Fish	LOEC	Fathead Minnow (Pimephales promelas)	> 13 mg/l (Embryo + 28 days post hatch) (highest concentration tested) (as free acid)
	NOEC	Fathead Minnow (Pimephales promelas)	13 mg/l (Embryo + 28 days post hatch) (highest concentration tested) (as free acid)
		Rainbow trout,donaldson trout (Oncorhynchus mykiss)	1099,6 mg/l, 96 h (highest concentration tested) (as free acid)
12.2. Persistence and degradability		Hydrolysis: <10% degradation at 50C for 5 days in pH4, 7, and 9 buffers Ready Biodegradability: 20% of theoretical C was released as CO2 over 29 day incubation Biodegradation (sludge): >99% disappearance when incubated with 1.5 g/L sludge solids (24 hrs) Degradation in sludge: After 1 hr incubation 90% of pemetrexed had disappeared. Numerous degradation peaks were observed by HPLC/RAM. 18.4% applied radioactivity evolved as 14 CO2 over the 28-day study. Degradation in water-sediment systems: DT50 (days): <0.5 Over 100 day study, 8.1 to 14.3% AR evolved as 14 CO2 Non extractable radioactive residues at Day 100: 100: 26.9% to 39.8% of applied radioactivity.Three major degradation products observed over 100 day study all of which were degraded over the duration of the study.	
12.3. Bioaccumulative potential		No data available on bioaccumulation.	
Partition coefficient n-octanol/water (log Kow)			
Pemetrexed Disodium Heptahydrate		< 1 (HPLC) Estimated	

Bioconcentration factor (BCF) Not available.

12.4. Mobility in soil No data available.

12.5. Results of PBT and vPvB assessment Chemical Safety Assessment is not required for this substance.

12.6. Other adverse effects Not available.

12.8. Ecotoxicological Properties

Drinking Water

Components	Test results
Pemetrexed Disodium Heptahydrate	0,045 µg/l, (as disodium salt)

Chronic Exposure of Aquatic Organisms

Components	Test results
Pemetrexed Disodium Heptahydrate	1 µg/l, (as disodium salt)

Acute Exposure of Aquatic Organisms

Components	Test results
Pemetrexed Disodium Heptahydrate	16 mg/l, (as disodium salt)

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Disposal methods/information 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

ADR

Not regulated as dangerous goods.

RID

Not regulated as dangerous goods.

ADN

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not applicable.

SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

EU regulations

Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex I

Not listed.

Regulation (EC) No. 1005/2009 on substances that deplete the ozone layer, Annex II

Not listed.

Regulation (EC) No. 850/2004 On persistent organic pollutants, Annex I as amended

Not listed.

Regulation (EC) No. 1907/2006, REACH Article 59(1) Candidate List as currently published by ECHA

Not listed.

Authorisations

Regulation (EC) No. 1907/2006, REACH Annex XIV Substances subject to authorization, as amended

Not listed.

Restrictions on use

Regulation (EC) No. 1907/2006, REACH Annex XVII Substances subject to restriction on marketing and use as amended

Not listed.

Directive 2004/37/EC: on the protection of workers from the risks related to exposure to carcinogens and mutagens at work

Not listed.

Other EU regulations

Directive 96/82/EC (Seveso II) on the control of major-accident hazards involving dangerous substances

Not listed.

Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work

Not listed.

Other regulations

The product is classified and labelled in accordance with EC directives or respective national laws
Young people under 18 years old are not allowed to work with this product according to the EU
Directive 94/33/EC on the protection of young people at work.
Pregnant women should not work with the product, if there is the least risk of exposure.

National regulations

Not available.

15.2. Chemical safety assessment

Not applicable.

SECTION 16: Other information

List of abbreviations

LAEG: Lilly Aquatic Exposure Guideline
LEG: Lilly Exposure Guideline
LOEC: Lowest Observed Effect Concentration
NOEC: No Observed Effect Concentration
TWA: Time Weighted Average

Information on evaluation method leading to the classification of mixture

The classification for health and environmental hazards is derived by a combination of calculation methods and test data, if available.

Full text of any statements or R-phrases and H-statements under Sections 2 to 15

R38 Irritating to skin.
R60 May impair fertility.
R61 May cause harm to the unborn child.
R68 Possible risk of irreversible effects.
H315 Causes skin irritation.
H341 Suspected of causing genetic defects.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs (<@1>) through prolonged or repeated exposure.

Lilly Lab Code

Health: 2
Fire: 1
Reactivity: 0
Special 1: R

Revision information

None.

Disclaimer

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 MERCHANT ABILITY 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.

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