SAFETY DATA SHEET

1. Identification

Product identifier **Alimta®**

Other means of identification

Item Code VL7623, VL7640

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

Recommended use Pharmaceutical

Recommended restrictions None known.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name Eli Lilly and Company

Address Lilly Corporate Center
Indianapolis, IN 46285
United States

Telephone Phone: +1-317-276-2000

E-mail lilly_msds@lilly.com

Emergency phone number CHEMTREC: +1-800-424-9300

2. Hazard(s) identification

Physical hazards Not classified.

Health hazards

Skin corrosion/irritation	Category 2
Germ cell mutagenicity	Category 2
Reproductive toxicity	Category 1A
Specific target organ toxicity, repeated exposure	Category 1

OSHA defined hazards Not classified.

Label elements

Signal word Danger

Hazard statement

H315	Causes skin irritation.
H341	Suspected of causing genetic defects.
H360	May damage fertility or the unborn child.
H372	Causes damage to organs (Blood) through prolonged or repeated exposure.

Precautionary statement

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.

Storage Not available.

Disposal Not available.

Hazard(s) not otherwise classified (HNOC) None known.

Supplemental information None.

3. Composition/information on ingredients

Mixtures

Chemical name	Common name and synonyms	CAS number	%
Pemetrexed Disodium Heptahydrate	disodium (2S)-2-[({4-[2-(2-amino-4-oxo-4,7-dihydro-3 H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]phenyl}c arbonyl)amino]pentanedioate hydrate L-Glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo-1H-pyrr olo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl]-, disodium salt, heptahydrate	357166-29-1	50

Composition comments Remaining components of this product are non-hazardous and/or are present at concentrations below reportable levels.

4. 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.

Most important symptoms/effects, 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.

Indication of 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.

5. Fire-fighting measures

Suitable extinguishing media Carbon dioxide, dry chemical or water.

Unsuitable extinguishing media None known.

Specific hazards arising from the chemical Hazardous decomposition products formed under fire conditions.

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

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures Wear suitable protective clothing, gloves and eye/face protection. See Section 8 of the SDS for Personal Protective Equipment.

Methods and materials 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.

Environmental precautions

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

7. Handling and storage

Precautions for safe handling

Provide adequate ventilation. Avoid contact with eyes, skin, and clothing. Wash hands thoroughly after handling. See Section 8 of the SDS for Personal Protective Equipment.

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.

8. Exposure controls/personal protection

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).

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

Eye/face protection

Wear goggles/face shield.

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. Select respirator with appropriate protection factor. Select appropriate respirator for physical characteristics of material.

Thermal hazards

Not available.

General hygiene considerations

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 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.

In production settings, airline-supplied, hood-type respirators are preferred. Shower and change clothing if skin contact occurs.

9. Physical and chemical properties

Appearance

Physical state

Solid.

Form

Solid. (Lyophilized).

Color	White.
Odor	Odorless
Odor 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.
Vapor pressure	No data available.
Vapor density	No data available.
Relative density	No data available.
Solubility(ies)	
Solubility (water)	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.
Other information	
Density	No data available.
Explosive properties	Not explosive
Oxidizing properties	The substance or mixture is not classified as oxidizing.
Percent volatile	No data available.
VOC (Weight %)	No data available.
9.2. Other information	
Minimum Ignition Temperature	No data available.

10. Stability and reactivity

Reactivity	Not water reactive.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	Hazardous polymerization does not occur.
Conditions to avoid	None known.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.

11. Toxicological information

Information on toxicological effects

Acute toxicity

Components	Species	Test Results
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)		
Acute		
Dermal		
LD	Rabbit	> 1000 mg/kg
Oral		
LD	Rat	> 500 mg/kg , (as free base)
Other		
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 or skin sensitization

Respiratory sensitization Due to lack of data the classification is not possible.

Skin sensitization 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.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

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.

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

12. Ecological information

Ecotoxicity

Components		Species	Test Results
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)			
Acute			
	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)
Chronic			
	LOEC	Midge (Chironomus riparius)	> 100000 µg/l, 28 h (highest concentration tested)

Components		Species	Test Results
	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			
Acute			
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)
Chronic			
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)

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.

Bioaccumulative potential No data available on bioaccumulation.

Partition coefficient n-octanol / water (log Kow)

Pemetrexed Disodium Heptahydrate	< 1 (HPLC) Estimated

Mobility in soil No data available.

Other adverse effects Not available.

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)

13. Disposal considerations

Disposal instructions 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.

14. Transport information

DOT

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

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

15. Regulatory information

US federal regulations This product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.
One or more components are not listed on TSCA.

CERCLA/SARA Hazardous Substances - Not applicable.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories Immediate Hazard - Yes
Delayed Hazard - Yes
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

US state regulations California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins.

US. California Controlled Substances. CA Department of Justice (California Health and Safety Code Section 11100)

Not listed.

US. Massachusetts RTK - Substance List

Not regulated.

US. New Jersey Worker and Community Right-to-Know Act

Not listed.

US. Pennsylvania Worker and Community Right-to-Know Law

Not listed.

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

Not Listed.

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Canada	Domestic Substances List (DSL)	No
Canada	Non-Domestic Substances List (NDSL)	No
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)
A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date 11-20-2014

Version # 01

Lilly Lab Code
Health: 2
Fire: 1
Reactivity: 0
Special 1: R

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

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