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

LY Number LY231514

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.
P260 Do not breathe dust.
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-3H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]phenyl}carbonyl)amino]pentanedioate hydrate 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	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). Pemetrexed is not light sensitive. Keep in original container.

8. Exposure controls/personal protection

Occupational exposure limits

Lilly (LEG)

Components	Type	Value
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)	TWA (12hrs)	0.3 ug/m3
	TWA (8hrs)	0.3 ug/m3

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

Exposure guidelines Health Based Excursion Limit: Maintain Full Shift TWA

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. Respirator selection must be based on known or anticipated exposure levels, the hazards of the product and the safe working limits of the respirator.

Thermal hazards Not available.

General hygiene considerations 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 9) (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	Not oxidizing.
Percent volatile	No data available.
VOC	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.

IARC Monographs. Overall Evaluation of Carcinogenicity

Not listed.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1052)

Not regulated.

US. National Toxicology Program (NTP) Report on Carcinogens

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 Harmful to aquatic life.

Components		Species	Test Results
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)			
	EbC50	Algae (Pseudokirchneriella subcapitata)	17 mg/l, 72 h (as free acid) (OECD 201)
	EC50	Respiration inhibition of activated sludge	> 1000 mg/l, 3 h (highest concentration tested) (as free acid) (OECD 209)
	ErC50	Algae (Pseudokirchneriella subcapitata)	63 mg/l, 72 h (as free acid) (OECD 201)
	LOEC	Algae (Pseudokirchneriella subcapitata)	27 mg/l (growth rate) (as free acid) (OECD 201)
			11 mg/l (yield) (as free acid) (OECD 201)
		Midge (Chironomous riparius)	> 100 mg/kg, 28 d (highest concentration tested) (free acid) (OECD 218)
	NOEC	Algae (Pseudokirchneriella subcapitata)	11 mg/l (growth rate) (as free acid) (OECD 201)
			4 mg/l (yield) (as free acid) (OECD 201)
		Midge (Chironomus riparius)	100 mg/kg, 28 d (highest concentration tested) (free acid) (OECD 218)
Aquatic			
Crustacea	EC50	Daphnia magna	462 mg/l, 48 h (as free acid) (OECD 202)
	LOEC	Daphnia magna	2.1 mg/l, 21 d (reproduction) (as free acid) (OECD 211)
	NOEC	Daphnia magna	1.2 mg/l, 21 d (reproduction) (as free acid) (OECD 211)
Fish	LC50	Rainbow trout,donaldson trout (Oncorhynchus mykiss)	> 1099.6 mg/l, 96 h (highest concentration tested) (as free acid) (OECD 203)
	LOEC	Fathead Minnow (Pimephales promelas)	> 13 mg/l (embryo + 28 days post hatch) (highest concentration tested) (as free acid) (OECD 210)

Components		Species	Test Results
	NOEC	Fathead Minnow (Pimephales promelas)	13 mg/l (embryo + 28 days post hatch) (highest concentration tested) (as free acid) (OECD 210)

A LAEG is the maximum allowable concentration at the point of application that is expected to result in no appreciable risk to populations of aquatic and terrestrial organisms, or to human health.

LILLY AQUATIC EXPOSURE GUIDELINES:

Pemetrexed Disodium Heptahydrate

Drinking water LAEG (at the point where surface water is taken for drinking water):	0.075 µg/l
Chronic LAEG (at the edge of the chronic mixing zone):	0.54 µg/l
Acute LAEG (at the edge of the acute mixing zone):	17000 µg/l

Persistence and degradability Stable in water: less than 10% hydrolysis in pH 4, 7, 9 buffers at 50C (OECD 105)
Not ready biodegradable: only 20% of theoretical released as CO2 over 29 days (OECD 301)
Degradable in sewage sludge: DT50 < 1 day; numerous degradation peaks observed (OECD 302)
Degradable in water-sediment systems: DT50 < 0.5 days, major degradation products degraded over 100 day study (OECD 308)

Bioaccumulative potential No data available on bioaccumulation. Potential to bioaccumulate is low.

Mobility in soil No data available.

Other adverse effects Not available.

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.

Toxic Substances Control Act (TSCA)

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 1910.1001-1052)

Not regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Classified hazard categories
Skin corrosion or irritation
Germ cell mutagenicity
Reproductive toxicity
Specific target organ toxicity (single or repeated exposure)

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.

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.

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

Revision date 02-18-2019

Version # 08

List of abbreviations

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

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 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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