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.
3. Composition/information on ingredients

Mixtures

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Common name and synonyms</th>
<th>CAS number</th>
<th>%</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Lilly (LEG) Components</th>
<th>Type</th>
<th>Value</th>
<th>Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemetrexed Disodium</td>
<td>Excursion Limit</td>
<td>3.6 ug/m³</td>
<td>30 minutes</td>
</tr>
<tr>
<td>Heptahydrate (CAS 357166-29-1)</td>
<td>TWA (12hrs)</td>
<td>0.3 ug/m³</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TWA (8hrs)</td>
<td>0.3 ug/m³</td>
<td></td>
</tr>
</tbody>
</table>

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

Chemical-resistant gloves and impermeable body covering to minimize skin contact.

Hand protection

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

Material name: Alimta®

5082 Version #: 01 Issue date: 11-20-2014
Components | Species | Test Results
--- | --- | ---
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)

**Acute**
- **Dermal**
  - LD: Rabbit
    - LD: > 1000 mg/kg

- **Oral**
  - LD: Rat
    - LD: > 500 mg/kg, (as free base)

- **Other**
  - LD50: Rat
    - LD50: > 1574 mg/kg, Intravenous (female), Convulsions. Mortality.
    - LD50: 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 corticosteroid (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.

- 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**

<table>
<thead>
<tr>
<th>Components</th>
<th>Species</th>
<th>Test Results</th>
</tr>
</thead>
</table>
Pemetrexed Disodium Heptahydrate (CAS 357166-29-1)

**Acute**
- EC50: Algae (Pseudokirchnerella subcapitata)
  - EC50: 63 mg/l, 72 h (average specific growth rate) (as free acid)
  - EC50: 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)
<table>
<thead>
<tr>
<th>Components</th>
<th>Species</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOEC</td>
<td>Algae (Pseudokirchnerella subcapitata)</td>
<td>11 mg/l, 72 h (average specific growth rate) (as free acid)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 mg/l, 72 h (yield) (as free acid)</td>
</tr>
<tr>
<td>NOEC</td>
<td>Midge (Chironomus riparius)</td>
<td>100000 µg/l, 28 h (highest concentration tested)</td>
</tr>
</tbody>
</table>

**Aquatic**

**Acute**

<table>
<thead>
<tr>
<th>Species</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphnia magna</td>
<td>EC50 462 mg/l, 48 h (as free acid)</td>
</tr>
<tr>
<td>Daphnia magna</td>
<td>NOEC 91.8 mg/l, 48 h (as free acid)</td>
</tr>
<tr>
<td>Rainbow trout, donaldson trout (Oncorhynchus mykiss)</td>
<td>LC50 &gt; 1099.6 mg/l, 96 h (highest concentration tested) (as free acid)</td>
</tr>
</tbody>
</table>

**Chronic**

<table>
<thead>
<tr>
<th>Species</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daphnia magna</td>
<td>EC50 1.8 mg/l, 21 d (reproduction) (as free acid)</td>
</tr>
<tr>
<td>Daphnia magna</td>
<td>LOEC 2.1 mg/l, 21 d (as free acid)</td>
</tr>
<tr>
<td>Daphnia magna</td>
<td>NOEC 1.2 mg/l, 21 d (as free acid)</td>
</tr>
<tr>
<td>Fathead Minnow (Pimephales promelas)</td>
<td>LOEC &gt; 13 mg/l (Embryo + 28 days post hatch) (highest concentration tested) (as free acid)</td>
</tr>
<tr>
<td>Fathead Minnow (Pimephales promelas)</td>
<td>NOEC 13 mg/l (Embryo + 28 days post hatch) (highest concentration tested) (as free acid)</td>
</tr>
<tr>
<td>Rainbow trout, donaldson trout (Oncorhynchus mykiss)</td>
<td>NOEC 1099.6 mg/l, 96 h (highest concentration tested) (as free acid)</td>
</tr>
</tbody>
</table>

**Persistence and degradability**

- Hydrolysis: <10% degradation at 50°C for 5 days in pH 4, 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)
- 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: 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)**

<table>
<thead>
<tr>
<th>Material</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemetrexed Disodium Heptahydrate</td>
<td>&lt; 1 (HPLC) Estimated</td>
</tr>
</tbody>
</table>

**Mobility in soil**

No data available.

**Other adverse effects**

Not available.

**Ecotoxicological Properties**

**Drinking Water**

<table>
<thead>
<tr>
<th>Components</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemetrexed Disodium Heptahydrate</td>
<td>0.045 µg/l, (as disodium salt)</td>
</tr>
</tbody>
</table>

**Chronic Exposure of Aquatic Organisms**

<table>
<thead>
<tr>
<th>Components</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemetrexed Disodium Heptahydrate</td>
<td>1 µg/l, (as disodium salt)</td>
</tr>
</tbody>
</table>
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.

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 11010)
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

<table>
<thead>
<tr>
<th>Country(s) or region</th>
<th>Inventory name</th>
<th>On inventory (yes/no)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>Domestic Substances List (DSL)</td>
<td>No</td>
</tr>
<tr>
<td>Canada</td>
<td>Non-Domestic Substances List (NDSL)</td>
<td>No</td>
</tr>
<tr>
<td>United States &amp; Puerto Rico</td>
<td>Toxic Substances Control Act (TSCA) Inventory</td>
<td>No</td>
</tr>
</tbody>
</table>

*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

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 MERCHANTABILITY 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.

For additional information contact:
Eli Lilly and Company
Hazard Communication
+1-317-651-9533