

MATERIAL SAFETY DATA SHEET

1. Identification

Product identifier Pemetrexed for Injection

Other means of identification

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 None known

restrictions.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name Reliance Life Sciences Pvt. Ltd.

Address Dhirubhai Ambani Life Sciences Center (DALC),
R-282, TTC Area of MIDC, Thane – Belapur Road,
Rabale, Navi Mumbai – 400701,
Maharashtra, India.

Emergency phone number + 91-22-6767 8000

2. Composition/information on ingredients

Components	CAS number	Quantity
Pemetrexed Disodium hemi-pentahydrate	150399-23-8	500 mg
Mannitol	87-78-5	500 mg
Sodium hydroxide	1310-73-2	Q.s.
Hydrochloric acid	7647-01-0	Q.s.

3. 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 Category 1
exposure

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.
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Storage Not available.

Disposal Not available.

Hazard(s) not otherwise

classified (HNOC) None known.

Supplemental information None.

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 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 Hazardous decomposition products formed under fire

From the chemical conditions.

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

precautions for firefighters

6. Accidental release measures

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

Methods and materials for Use double pairs of latex disposable gloves which must
containment and be disposed of within an hour, goggles, impermeable body
cleaning up 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, Storage temperature: between 20 and 25 °C (68 to 77°F).

including any incompatibilities 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

Components	Type	Value	Form
Pemetrexed	Excursion Limit	3.6 ug/m3	30 minutes
Disodium hemi-pentahydrate	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 For appropriate handling precautions in specific laboratory or manufacturing operations, consultation with an occupational health and safety or technical services representative is recommended.

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.

GENERAL: For all work environments, wear eye protection and ELIMINATE hand-to-eye contact.

Avoid skin contact, wear gloves, and take other appropriate precautions.

Appropriate engineering Extensive local exhaust, ventilated enclosure (HEPA-filtered

Controls 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	In production settings, airline-supplied, hood-type respirators
Considerations	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 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 < 1.000

(n-octanol/water)

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 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 Hazardous decomposition products formed under fire

Products conditions.

11. Toxicological information

Information on toxicological effects

Acute toxicity

Components	Species	Test Results
Pemetrexed Disodium Hemi-pentahydrate Dermal Acute		

LD Oral	Rabbit	> 1000 mg/kg
LD Other	Rat	> 500 mg/kg , (as free base)
LD 50	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 Rabbit: Mild eye irritation. (cleared within 7 days)

Irritation Based on available data, the classification criteria are not met.

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

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 1910.1001-1050) 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.

12. Ecological information

Ecotoxicity Harmful to aquatic life.

Components		Species	Test Results
Pemetrexed Disodium Hemi-pentahydrate			
Aquatic	EC50	Respiration inhibition of activated sludge	> 1000 mg/l, 3 h (highest concentration tested) (as free acid) (OECD 209)
	LOEC	Midge (Chironomus riparius)	> 100 mg/kg, 28 d (highest concentration tested) (free acid) (OECD 218)

	NOEC	Midge (Chironomus riparius)	100 mg/kg, 28 d (highest concentration tested) (free acid) (OECD 218)
Algae	EbC50	Algae (Pseudokirchneriella subcapitata)	17 mg/l, 72 h (as free acid) (OECD 201)
	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)
	NOEC	Algae (Pseudokirchneriella subcapitata)	11 mg/l (growth rate) (as free acid) (OECD 201) 4 mg/l (yield) (as free acid) (OECD 201)
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)

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

Partition coefficient n-octanol / water (log K_{ow})

Pemetrexed Disodium Hemi-pentahydrate < 1 (HPLC) (estimation) (OECD 117)

Mobility in soil No data available.

Other adverse effects Not available.

13. Disposal considerations

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.

Disposal instructions

Waste from residues / unused products Not available.

Contaminated packaging Not available.

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 Not applicable.

Annex II of MARPOL 73/78 and the IBC Code

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 regulated.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Immediate Hazard - Yes

Delayed Hazard - Yes

Fire Hazard - No

Pressure Hazard - No

Reactivity Hazard - No

Hazard categories

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.

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

Revision date

Version #

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

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.

Disclaimer

Hazard(s) identification: Hazard statement

Exposure controls/personal protection: Exposure guidelines

Exposure controls/personal protection: General hygiene considerations

Physical & Chemical Properties: Multiple Properties

GHS: Classification

Revision information