

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 1 of 11

Section 1 - Identification

- (a) **Product Identifier:** Pemetrexed for Injection, USP
- (b) **Product Code:** 70860-202
70860-203
- Common/Trade Name:** Pemetrexed for Injection, USP
- Chemical Name:** L-glutamic acid, *N*-[4-[2-(2-amino-4,7-dihydro-4-oxo-1*H*-pyrrolo[2,3-*d*]pyrimidin-5yl)ethyl]benzoyl]-, disodium salt, hemipentahydrate
- Chemical Family:** Folate Analog Metabolic Inhibitor
- (c) **Product Use:** Pharmaceutical, Injectable
- Product Type:** Regulated Prescription Drug
- Container Information:** Vial
- (d) **Distributor:** Athenex Pharmaceutical Division, 10 N. Martingale Road, Suite 230, Schaumburg, IL 60173, 847-886-9515
- (e) **Emergency Telephone:** 855-273-0154

Section 2 - Hazards Identification


(a)	Classification:	Hazard Identification: Not Classified Physical Hazards/Health Hazards: Skin corrosion/irritation: Category 2 Germ cell mutagenicity: Category 2 Reproductive toxicity: Category 1A Specific target organ toxicity: Category 1
(b)	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
	Symbols	

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 2 of 11

	Precautionary Statement(s)	<p>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.</p> <p>Response P308 + P313 If exposed or concerned: Get medical advice/attention.</p> <p>Storage Not available.</p> <p>Disposal Not available.</p>
(c)	Description of Hazards	N/A
(d)	Unknown Acute Toxicity	N/A

Section 3 – Composition / Information on Ingredients

(a) Chemical Name	(b) Common Name / Synonym	Composition of 100 mg/Vial	Composition of 500 mg/Vial	(c) CAS No.	(d) Impurities / Stabilizing Additives
L-glutamic acid, <i>N</i> -[4-[2-(2-amino-4,7-dihydro-4-oxo-1 <i>H</i> -pyrrolo[2,3- <i>d</i>]pyrimidin-5yl)ethyl]benzoyl]-, disodium salt, hemipentahydrate	Pemetrexed Disodium	120.8 mg	604.2 mg	357166-30-4	N/A
Mannitol, USP	Mannitol, USP	106 mg	500 mg	69-65-8	N/A
Sodium Hydroxide, USP	Sodium Hydroxide	q.s. to pH 7.4 ± 0.3	q.s. to pH 7.4 ± 0.3	1310-73-2	N/A
Hydrochloric Acid, USP	Hydrochloric Acid	q.s. to pH 7.4 ± 0.3	q.s. to pH 7.4 ± 0.3	7647-01-0	N/A


 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 3 of 11

Section 4 – First Aid Measures

Eye Exposure:	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.
Skin Exposure:	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.
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.
Inhalation:	Remove to fresh air. If breathing stops, provide artificial respiration. Get medical attention 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.
Notes to Physician:	See package insert for more information.

Section 5 – Fire-fighting Measures

- (a) **Extinguishing Media** Carbon dioxide, dry chemical or water.
- (b) **Hazardous Decomposition Products:** Hazardous decomposition products formed under fire conditions.

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 4 of 11

- (c) **Special Protective Equipment / Precautions:** Wear self-contained breathing apparatus and protective clothing.

Section 6 - Accidental Release Measures

Spill: 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.

Release to Air: N/A.

Release to Water: Avoid discharge into drains, water courses or onto the ground.

Section 7 - Handling and Storage

General 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.


Storage Conditions: Store powder at 25°C (77°F); excursions permitted between 15° and 30°C (59° and 86°F). [See USP Controlled Room Temperature.]

Section 8 - Exposure Controls / Personal Protection

Exposure Limits: Component	Type	Value	Form
Pemetrexed Disodium	Excursion Limit	3.6 ug/m ³	30 minutes
	TWA (12 hrs)	0.3 ug/m ³	
	TWA (8 hrs)	0.3 ug/m ³	

Engineering Controls

Ventilation: Extensive local exhaust, ventilated enclosure (HEPA-filtered balance enclosure, fume hood, or Class II or III vertical flow biosafety cabinet), or enclosed process equipment.


 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 5 of 11

Individual Protection Measures

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.
Eye Protection:	Wear goggles/face shield.
Skin 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.
Additional Exposure Precautions:	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.

Section 9 - Physical and Chemical Properties

(a)	Appearance	White-to-light yellow or green-yellow lyophilized powder.
(b)	Odor	Not available
(c)	Odor Threshold	Not available
(d)	pH	7.4 ± 0.3
(e)	Melting Point:	Not available
(f)	Initial Boiling Point:	Not available
(g)	Flash Point	Not available
(h)	Evaporation Rate:	Not available
(i)	Flammability	Not available
(j)	Upper Lower Flammability or Explosion Limits	Not available
(k)	Vapor Pressure:	Not available
(l)	Vapor Density:	Not available
(m)	Relative Density	Not available
(n)	Solubility(ies)	89.4 g/l, (pH 9), (as free acid) 101.5 g/l, (pH 7), (as free acid)
(o)	Partition Coefficient: n-octanol/water	< 1.000

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 6 of 11

(p)	Auto-ignition Temperature	Not available
(q)	Decomposition Temperature	Not available
(r)	Viscosity	Not available

Section 10 - Stability and Reactivity


(a)	Reactivity	Stable under normal conditions of use.
(b)	Chemical Stability	Stable at normal temperatures and pressures
(c)	Possibility of Hazardous Reactions	Hazardous polymerization does not occur
(d)	Conditions to Avoid	Not established
(e)	Incompatible Materials	Strong oxidizing agents.
(f)	Hazardous Decomposition Products	Hazardous decomposition products formed under fire conditions.

Section 11 - Toxicological Information

(a)	Likely Routes of Exposure	Inhalation, ingestion.
(b)	Symptoms related to the physical, chemical and toxicological characteristics	No data available.
(c)	Delayed and immediate effects and also chronic effects from short and long term exposure	No data available.

a) Acute Toxicity

Component	Type	Route	Species	Dosage
Pemetrexed Disodium	LD	Oral	Rat	>500mg/kg (as free base)
	LD	Dermal	Rabbit	>1000 mg/kg
	LD ₅₀	Intravenous	Rat	> 1574 mg/kg (female), Convulsions, Mortality. 1332 mg/kg (male), convulsions.

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 7 of 11


b) Hazardous Chemical Listings

NTP: Not Listed	IARC: Not Listed	OSHA: Not Listed	ACGIH: Not Listed
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Due to lack of data, carcinogenicity classification is not possible.

Section 12 - Ecological Information

(a) Ecotoxicity	<i>Acute</i>	EC50	Algae (Pseudokirchnella 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		>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 (Pseudokirchnere lla 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)
	<i>Chronic Crustacea</i>	EC50	Daphnia magna	1.8 mg/l, 21 d (reproduction) (as free acid)

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 8 of 11

		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)
(b)	Persistence and degradability	<p>Hydrolysis: <10% degradation at 50C for 5 days in pH4, 7, and 9 buffers</p> <p>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)</p> <p>Degradation in sludge:</p> <p>After 1 hr incubation 90% of pemetrexed had disappeared. Numerous degradation peaks were observed by HPLC/RAM.</p> <p>18.4% applied radioactivity evolved as 14 CO₂ over the 28-day study. Degradation in water-sediment systems:</p> <p>DT50 (days): <0.5</p> <p>Over 100-day study, 8.1 to 14.3% AR evolved as 14 CO₂</p> <p>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.</p>		
(c)	Bioaccumulative potential	No data available on bioaccumulation.		
(d)	Mobility in soil	Not available.		
(e)	Other Adverse Effects	Not available.		

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 9 of 11

Section 13 - Disposal Considerations

Waste Disposal: 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 per all applicable laws and regulations, e.g., secure chemical landfill disposal.

Section 14 - Transport Information

Not regulated for transport under USDOT, IATA, or IMDG regulations.

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Athenex Pharmaceutical Division usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations:

- TSCA – Not regulated
- CERCLA - Not on this list
- SARA 304 - Not on this list
- SARA 313 - Not on this list
- OSHA – Not on this list


Section 16 - Other Information

As of the date of effectiveness, 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 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:


Athenex Pharmaceutical Division
 10 N. Martingale Road, Suite 230
 Schaumburg, IL 60173
 847-886-9515

Glossary: This glossary contains definitions of general terms used in SDSs. Not all of these

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 10 of 11

Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AICS	Australian Inventory of Chemical Substances
AIHA	American Industrial Hygiene Association
ANSI	American National Standards Institute
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
DSL	Domestic Substances List
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of Notified Chemical Substances
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEPA	High Efficiency Particulate Air (Filter)
HMIS	Hazardous Materials Identification System
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NDSL	Non-Domestic Substances List
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPDES	National Pollutant Discharge Elimination System
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations

 Pharmaceutical Division	Pemetrexed for Injection, USP		Safety Data Sheet (SDS)	
	Effective Date: 18APR2022	SDS No.: SDS052	Revision No: 01	Page 11 of 11

USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)
WHMIS	Workplace Hazardous Materials Information System

Signature Manifest

Document Number: SDS052

Revision: 01

Title: Pemetrexed for Injection, USP

Effective Date: 05 May 2022

All dates and times are in Eastern Standard Time.

Pemetrexed for Injection, USP

Change Request

Name/Signature	Title	Date	Meaning/Reason
Mica Downey (MDOWNEY)	Director of Validations	11 Apr 2022, 11:55:33 AM	Approved

Dept Approval

Name/Signature	Title	Date	Meaning/Reason
John Andre (EXT-JANDRE)	Regulatory Affairs Consultant	11 Apr 2022, 03:56:18 PM	Approved

Final QA Approval/Set Effective Date

Name/Signature	Title	Date	Meaning/Reason
Lori Aleshin (LALESHIN)	Director of Quality Assurance	05 May 2022, 03:58:56 PM	Approved