

MATERIAL SAFETY DATA SHEET

Version No: MSDS/Pem-AUS/DP-002

Effective Date: 03rd August 2017

Pemetrexed Disodium Powder for Injection, 100 mg/vial, 500 mg/vial and 1000 mg/vial

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Pemetrexed Disodium Powder for Injection, 100 mg/vial, 500 mg/vial and 1000 mg/vial

Sponsor	Manufacturer
Accord Healthcare Pty Ltd Level 24, 570 Bourke Street, Melbourne, VIC, 3000, Australia	Intas Pharmaceuticals Ltd. Plot No. 5, 6 and 7, Pharmez, Near Matoda Village, Ahmedabad-382 213, Gujarat, India

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: Pemetrexed disodium (Hemi pentahydrate).

Inactive: Mannitol, Sodium hydroxide, Hydrochloric Acid

SECTION 3 - HAZARDS IDENTIFICATION

Emergency Overview

Primary Physical and Health Hazards: Mutagen. Irritant (eyes, skin). Reproductive, Blood and Bone Marrow Effects.

Caution Statement: Pemetrexed Disodium for Injection alters genetic material and may be irritating to the eyes and skin. Effects of exposure may include reproductive tissue changes, fetal changes, decreased fetal weight, decreased offspring survival, decreased blood cell counts, and lymphoid tissue and bone marrow changes.

Appearance: White lyophilized plug

Physical State: Solid

Odor: Odorless

Routes of Entry: Inhalation and skin contact.

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Effects of Overexposure: May be irritating to the eyes and skin. Decreased fetal weight and viability have been reported in animal studies with pemetrexed disodium. Pemetrexed is a folic acid antimetabolite, this class of compounds is known to cause developmental effects. 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.

Patients are instructed to take folic acid and vitamin B12 to reduce treatment-related toxicity. Skin rash has been reported in patients not pretreated with a cortiosteroid (dexamethasone).

Medical Conditions Aggravated by Exposure: None known.

Carcinogenicity:

Pemetrexed disodium - Not listed by IARC, NTP, ACGIH, or OSHA.

Mannitol - Not listed by IARC, NTP, ACGIH, or OSHA. Two-year dietary studies demonstrated no evidence of carcinogenicity in mice and rats.

SECTION 4 - FIRST AID MEASURES

Eyes: Hold eyelids open and flush with a steady, gentle stream of water for 15 minutes. See an ophthalmologist (eye doctor) or other physician immediately.

Skin: Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with plenty of soap and water. Get medical attention if irritation develops.

Inhalation: Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

Ingestion: Do not induce vomiting. Call a physician or poison control center. If available, administer activated charcoal (6-8 heaping teaspoons) with two to three glasses of water. Do not give anything by mouth to an unconscious person. Immediately transport to a medical care facility and see a physician.

Notes to Physician:

Pemetrexed disodium - 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.

SECTION 5 - FIRE FIGHTING MEASURES

Flash Point: No applicable information found

UEL: No applicable information found

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LEL: No applicable information found

Extinguishing Media: Use water, carbon dioxide, dry chemical, foam, or Halon.

Unusual Fire and Explosion Hazards: As a finely divided material, may form dust mixtures in air which could explode if subjected to an ignition source.

Hazardous Combustion Products: May emit toxic fumes when exposed to heat or fire.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Spills: 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.

SECTION 7 - HANDLING AND STORAGE

Storage Conditions: Store at Controlled Room Temperature 20 to 25 C (68 to 77 F) [see USP]. Pemetrexed is not light sensitive.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

For appropriate handling precautions in specific laboratory, manufacturing, or clinical health care operations, consult with a health and safety or technical services representative.

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

Respiratory Protection: When the exposure guidelines may be exceeded, use an approved HEPA filtered or supplied-air respirator.

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Eye Protection: Chemical goggles and/or face shield.

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.

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

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Appearance: White lyophilized plug

Odor: Odorless

Boiling Point: No applicable information found

Melting Point: No applicable information found

Density: No applicable information found

pH: No applicable information found

Evaporation Rate: No applicable information found

Water Solubility: Soluble

Vapor Density: No applicable information found

Vapor Pressure: No applicable information found

SECTION 10 - STABILITY AND REACTIVITY

Stability: Stable at normal temperatures and pressures.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).

Hazardous Decomposition: May emit toxic fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

SECTION 11 - TOXICOLOGY INFORMATION

Acute Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

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Oral:

Pemetrexed - Rat, 500 mg/kg, no deaths or toxicity.

Skin:

Pemetrexed disodium - Rabbit, 1000 mg/kg, no deaths.

Inhalation: No applicable information found.

Intravenous:

Pemetrexed disodium - Rat (male), median lethal dose 1332 mg/kg, convulsions.

Rat (female), median lethal dose greater than 1574 mg/kg, mortality, convulsions.

Skin Contact:

Pemetrexed disodium - Rabbit, irritant

Eye Contact:

Pemetrexed disodium - Rabbit, mild irritant

Chronic Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Target Organ Effects:

Pemetrexed disodium - 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.

Reproduction:

Pemetrexed disodium - 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.

Sensitization: No applicable information found.

Mutagenicity:

Pemetrexed disodium - Clastogenic in the in vivo micronucleus assay in the mouse, but was negative in the in vitro chromosome aberration test in Chinese hamster ovary cells. Negative in the Ames test.

SECTION 12 - ENVIRONMENTAL IMPACT INFORMATION
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No environmental data for the mixture or formulation. The environmental information for ingredient(s) or related material(s) are presented.

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Ecotoxicity Data:

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Rainbow trout 96-hour median effective concentration: >1212.7 mg/L

Daphnia magna 48-hour median effective concentration: 509.5 mg/L

Green algae (*S. capricornutum*) 72-hour median effective concentration (average specific growth rate): 210 mg/L

Activated sludge respiration inhibition 3-hour median effective concentration: >122 mg/L

Environmental Fate:

Pemetrexed disodium

Log Kow: <1

Bioconcentration factor: <4.6

Dissociation constants in 66% DMF/water (pKa): <3.5, 6.24, 7.61, and >13.5

Biodegradation half-life (1.5 g solids/L): <3.9 hours

Biodegradation half-life (0.15 g solids/L): >24 hours

Amount associated with municipal sludge solids: none

Environmental Summary:

Pemetrexed disodium - Practically non-toxic to fish, aquatic invertebrates, green algae, and activated sludge microorganisms. No volatility expected. Low potential to bioconcentrate in aquatic organisms. Persistence in the environment not expected due to biodegradation.

SECTION 13 - DISPOSAL INFORMATION

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations. To avoid accidental exposure due to waste handling, place waste residue in a segregated, sealed plastic container.

SECTION 14 - TRANSPORTATION INFORMATION

Regulatory Organizations:

DOT: Not Regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

SECTION 15 - REGULATORY INFORMATION

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.

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U.S. Regulations

Pemetrexed disodium

TSCA - No

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

Mannitol

TSCA - Yes

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list

OSHA Substance Specific - No

EU Regulations

EC Classification

Contains pemetrexed disodium (C = 50%)

T (Toxic)

Xi (Irritant)

Mutagen Category 3

Reproductive Category 1

Risk Phrases

R 36/38 - Irritating to eyes and skin.

R 60 - May impair fertility.

R 61 - May cause harm to the unborn child.

R 68 - Possible risk of irreversible effects.

Safety Phrases

S 36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

S 53 - Avoid exposure -- obtain special instructions before use.

SECTION 16 - OTHER DATA

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.