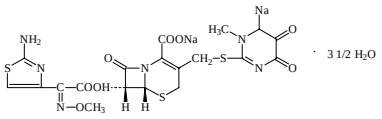
APOTEX
ADVANCING GENERICS

Material Safety Data Sheet

Section 1. Product Identification and Uses

Common/Trade name	**Ceftriaxone sodium**	**DSL#**	Not on the DSL list.
Synonyms	Cefatriaxone hydrate; Ceftriaxone sodium hydrate; Cephthriaxone	**CAS#**	104376-79-6
Chemical name	5-Thia-1-azabicyclo(4.2.0)oct-2-ene-2-carboxylic acid, 7-(((2-amino-4-thiazolyl)(methoxyimino)acetyl)amino)-8-oxo-3-(((1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-1,2,4-triazin-3-yl)thio)methyl)-,disodium salt, (6R-(6-alpha,7-beta(Z)))- hydrate (2:7) (6R-(6-alpha,7beta(Z)))-	**Molecular weight**	661.6 g/mole
Chemical family	Cephalosporin	**Chemical formula**	$C_{18}H_{16}N_8Na_2O_7S_3 \cdot 3.5\ H_2O$
Supplier	MSN Laboratories Ltd. Patancheru Mandal BMedak (Sist) A.P, 502329 India	**Chemical structure**	
Material uses	Pharmaceutical active ingredient. Therapeutic category: Antibacterial	**Manufacturer**	Not available
Emergency phone	**(416)-749-9300** ext. 5555 For general information call ext. 8483 (8 AM-4 PM)	**DIN**	Not applicable.

Section 2. Hazards Identification

Potential Acute Health Effects

Possible eye, skin, gastrointestinal and/or respiratory tract irritation.

Potential Chronic Health Effects

Possible hypersensitization, superinfections, antibiotic-associated pseudomembranous colitis, and pseudolithiasis.

WHMIS

Class D-2B: Material causing other toxic effects (Toxic).

Remark

Covered by Food & Drug Act and therefore not regulated under WHMIS

Apotex Hazard Classification (For Apotex internal practices only)

This material has been assigned hazard class: **1**

Section 3. First Aid Measures

Eye contact	IMMEDIATELY flush eyes with running water for at least 15 minutes, keeping eyelids open. Take care not to rinse contaminated water into the non-affected eye. Always seek medical attention for accidents involving the eyes.
Skin contact	Flush the contact area with lukewarm running water.
Hazardous skin contact	Flush the contact area with lukewarm running water for at least 15 minutes. Remove contaminated clothing, taking care not to spread the chemical. Seek medical attention if irritation persists.
Slight inhalation	Allow the victim to rest in a well ventilated area. If symptoms persist, obtain medical advice.

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Hazardous inhalation	Take proper precautions to ensure your own safety before attempting rescue. Remove source of contamination or move victim to fresh air. If breathing has stopped, trained personnel should begin artificial respiration (use protective mask with one-way valve), or if the heart has stopped, cardiopulmonary resuscitation (CPR) immediately. Seek medical attention.
Slight ingestion	Flush out mouth with water.
Hazardous ingestion	Never give anything by mouth if victim is rapidly losing consciousness, or is unconscious or convulsing. Rinse mouth thoroughly with water. If breathing has stopped, trained personnel should begin artificial respiration (use protective mask with one -way valve), or if the heart has stopped, cardiopulmonary resuscitation (CPR) immediately. Seek medical attention. Treatment of cephalosporin overdose should be symptomatic and supportive and may include the following: 1. Administer activated charcoal as a slurry. 2. For hypersensitivity reactions, manage anaphylaxis with establishment of patent airway, epinephrine, and diphenhydramine. 3. For seizures, administer intravenous diazepam or lorazepam. If seizures recur, consider phenobarbital. 4. For dysrhythmias, treat with standard antiarrhythmic drugs, if necessary. 5. Monitor fluid and electrolyte status in patients with severe vomiting and/or diarrhea. Monitor renal and hematologic abnormalities. 6. For coagulopathies, administer vitamin K. 7. For mild pseudomembranous colitis, treatment is usually NOT necessary. For moderate to severe pseudomembranous colitis, manage with fluids and electrolytes, protein supplementation, and treatment with an oral antibacterial drug effective against Clostridium difficile. (Meditext 2008 and USP DI 2008)

Section 4. Hazardous Ingredients

Name	CAS #	% (w/w)
Ceftriaxone sodium	104376-79-6	100

Toxicity values of the hazardous ingredients

Refer to Sec. 11.

TLV Industry: 0.02 mg/m3; STEL 0.06 mg/m^3

Section 5. Fire Fighting Measures

The product is:	May be combustible.
Autoignition temperature	Not available.
Fire degradation products	Decomposition products may include the following materials: carbon oxides (CO, CO_2), nitrogen oxides (NO, NO_2 etc.), sulfur oxides (SO_2, SO_3 etc.). Some metallic oxides.
Flash points	Not applicable.
Flammable limits	Not available.
Fire extinguishing procedures	Extinguisher media: water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials. Special fire fighting procedures: As with all fires, evacuate personnel to safe area. Firefighters should use self-contained breathing equipment and protective clothing.
Flammability	Emits toxic fumes under fire conditions.
	Remark No additional remark.
Risks of explosion	Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Fine airborne dust can be ignited by static discharge. As with all dry powders, it is advisable to ground mechanical equipment in contact with dry material to dissipate the potential buildup of static electricity.
	Remark No additional remark.

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Section 6. Accidental Release Measures

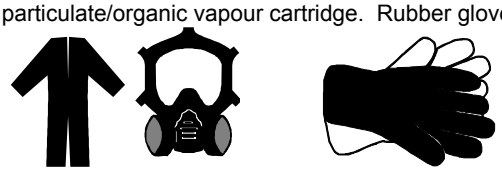
Spill and leak

Vacuum or sweep up spillage. Avoid dust. Place spillage into an appropriate labeled waste disposal container. Wash contaminated clothing before reuse. Ventilate area and wash spill site. Follow appropriate Safe Work Practices.

Protective Clothing Pictograms in case of large spill and/or high exposure levels

Protective clothing in case of large spill

Full suit with hood, or disposable/washable coveralls. Full facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge. Rubber gloves (impervious).



Section 7. Handling and Storage

Precautions

Use with adequate dust control. In case of insufficient ventilation, wear suitable respiratory equipment. Avoid inhalation, skin and eye contact. Wash thoroughly after handling. Store in a refrigerator.

Storage

Store in suitable labelled containers. Keep containers tightly closed when not in use and when empty. Protect from damage. Store in a refrigerator.

Section 8. Exposure Controls/Personal Protection

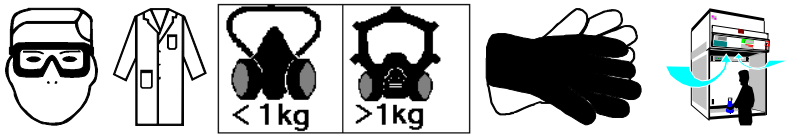
Engineering Controls

Exposure to this material can be controlled in many ways. The measures appropriate for a particular worksite depend on how this material is used and on the extent of exposure. This general information can be used to help develop specific control measures. Ensure that control systems are properly designed and maintained. Comply with occupational, environmental, fire, and other applicable regulations.
Engineering methods to control hazardous conditions are preferred. Methods include mechanical (local exhaust) ventilation, process or personnel enclosure and control of process conditions. Administrative controls and personal protective equipment may also be required. Supply sufficient replacement air to make up for air removed by exhaust system.

Personal Protection

Splash goggles. Full suit with hood, or disposable/washable coveralls. Full facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge (less then 1 kg). Powered Air Purifying Respirator (PAPR) with combination particulate/organic vapour cartridge (greater then 1 kg). Nitrile gloves (impervious). Chemical fume hood.

Protective Clothing (Pictograms)



PERSONAL PROTECTIVE EQUIPMENT:
If engineering controls and work practices are not effective in controlling exposure to this material, then wear suitable personal protective equipment, including approved respiratory protection. Have appropriate equipment available for use in emergencies such as spills or fire. If respiratory protection is required, institute a complete respiratory protection program, including selection, fit testing, training, maintenance and inspection. Refer to the CSA Standard Z94, "Selection, Care, and Use of Respirators".
RESPIRATORY PROTECTION GUIDELINES:
Where Local Exhaust Ventilation (LEV) at dust generating process points exists, respiratory protection may not be required.
When working with quantities less than 1 kg and in the absence of appropriate Local Exhaust Ventilation (LEV) with dusty processes, a full facepiece Air Purifying Respirator with combination particulate/organic vapour cartridge and goggles is recommended.
When working with quantities greater than 1 kg and in the absence of Local Exhaust Ventilation (LEV) with dusty processes, a Powered Air Purifying Respirator (PAPR) with combination particulate/organic vapour cartridge and helmet/hood or Supplied Air Respirator (SAR) is recommended.
The specific respirator selected must be based on contamination levels found in the work place, the specific operation and not exceed the working limits of the respirator.
When performing cleaning activities refer to appropriate cleaning solution MSDS.
EYE/FACE PROTECTION: Splash goggles/safety glasses.
PROTECTIVE CLOTHING/SKIN PROTECTION: Glove selection must take into account any solvents and other hazards present. The selection of gloves for a specific activity must be based on the material's properties and on possible permeation and degradation that may occur under the circumstances of use. Potential allergic reactions can occur with certain glove materials (e.g. Latex) and therefore these should be avoided. Full environmental suit with hood. and/or other resistant protective clothing when working in dusty areas. Have a safety shower/eye-wash fountain readily available in the immediate work area.
EXPOSURE CONTROLS/PERSONAL PROTECTION COMMENTS: In the event clothing becomes contaminated, remove promptly. Launder before use. Inform laundry personnel of contaminant's hazards. Do not eat, drink or smoke in work areas. Wash hands thoroughly after handling this material. Maintain good

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housekeeping.

Section 9. Physical and Chemical Properties

Physical state and appearance	Solid. (powder)	**Odor**	Not available.
pH	6.0 - 8.0 (10% solution)	**Taste**	Not available.
Odor threshold	Not available.	**Color**	Yellowish-orange
Volatility	Not available.		
Melting point/ Freezing point	>155°C (311°F) (decomposes)		
Boiling point	Not available.		
Specific gravity	Not available.		
Vapor density	Not available.		
Vapor pressure	Not available.		
Partition Coefficient:	n-octanol/water: 0.025 at pH2		
Ionicity (surface active agent)	Not available.		
Critical temperature	Not available.		
Instability temperature	Not available.		
Conditions of instability	No additional remark.		
Dispersion properties	See solubility.		
Evaporation rate	Not available.		
Solubility	Freely soluble in water. Sparingly soluble in methanol; very slightly soluble in alcohol.		

Section 10. Stability and Reactivity

Stability	The product is stable.
Hazardous decomp. products	Not available.
Degradability	Not available.
Corrosivity	Not corrosive
	Remark No additional remark.
Reactivity/ Incompatibility	Oxidizing agents. Avoid exposure to heat and moisture.
	Remark Not additional remark.

Section 11. Toxicological Information

Routes of entry	Ingestion. Inhalation.
Toxicity data	RTECS#: XI0368800 LD50: >10 gm/kg (oral-rat) LD50: >10 gm/kg (oral-mouse)

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Long-term effects

Possible hypersensitization, superinfections, antibiotic-associated pseudomembranous colitis, and pseudolithiasis.
Carcinogenicity: Not listed by IARC, NTP, ACGIH, or OSHA.
Reproductive Toxicity: Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.
Teratogenicity: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately 3 times the human dose. There are, however, no adequate and well- controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Mutagenicity: Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured in vitro with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Remark

Medical conditions aggravated by exposure: Hypersensitivity to material; active alcoholism or recent alcohol ingestion; allergies; history of bleeding disorders; concurrent kidney and liver function impairment; gallbladder disease; and gastrointestinal disease, especially ulcerative colitis, regional enteritis, or antibiotic-associated colitis. Persons allergic to one cephalosporin or cephamycin or to penicillins, penicillin derivatives, or penicillamine may be allergic to this material also.

Short-term effects and Signs & Symptoms of overexposure

Possible eye, skin, gastrointestinal and/or respiratory tract irritation.
The usual adult dose (by intravenous infusion) of ceftriaxone sodium is 1 to 2 grams (base) as a single daily dose, or in two equally divided doses every 12 hours, not to exceed a maximum of 4 grams per day.
Adverse effects of cephalosporins may include black, tarry stools; chest pain; chills; cough; fever; painful or difficult urination; shortness of breath; sore throat; sores, ulcers, or white spots on lips or in mouth; swollen glands; unusual bleeding or bruising; skin itching, rash, or redness; hives; abdominal or stomach pain or cramps; nausea or vomiting; diarrhea; headache; indigestion; flatulence; unusual tiredness or weakness; loss of appetite; dizziness; and vaginal itching, infection, or discharge. Possible allergic reaction to material if inhaled, ingested or in contact with skin.
Overdose effects of cephalosporins may include the adverse effects listed above and seizures.

Remark

The above adverse effects are based on clinical studies.

Section 12. Ecological Information

Ecological Information

This material is strongly toxic for microorganisms and barely toxic for fish, planktonic crustaceans, and algae.

Section 13. Disposal Considerations

Waste Disposal

For internal Apotex waste disposal: Collect in sealed containers and place in appropriate labeled pharmaceutical solid waste class 261N.
For external waste disposal: Follow all appropriate safe work procedures and federal, provincial and local regulations for disposal. Use only licensed disposal and waste hauling companies.

Section 14. Transport Information TDG, IATA, IMDG

Not controlled under TDG (Canada).

UN

Not applicable (PIN and PG).

Special Provisions for Transport

Not applicable.

Section 15. Other Regulatory Information and Pictograms

NATIONAL FIRE PROTECTION ASSOCIATION (NFPA) HAZARD INDEX

NFPA-HEALTH-blue :1-Slightly hazardous to health.
NFPA-FLAMMABILITY-red :1-Materials that must be preheated before ignition can occur.
NFPA-REACTIVITY-yellow :0-Normally stable.

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National Fire Protection Association (U.S.A.)

Health

Fire Hazard

Reactivity

Specific Hazard

Hazardous Material Information System (U.S.A.)

Health Hazard	1
Fire Hazard	1
Reactivity	0
Personal Protection	X

* - Chronic hazard indicator
X - See Section 8

HCS (Hazardous Communication System) (OHSA, U.S.A.)

Class: Harmful

DOT (Department of Transportation) (U.S.A) (Pictograms)

Not a DOT controlled material (United States).

EU Classification and Labelling

R36/37/38- Irritating to eyes, respiratory system and skin. R42/43- May cause sensitization by inhalation and skin contact. R53- May cause long-term adverse effects in the aquatic environment. S36- Wear suitable protective clothing.

ADR (European Agreement of Dangerous goods by Road) (Pictograms)

Not controlled under ADR (Europe).

Other Regulations

This product has been classified in accordance with the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

Section 16. Other Information

References

The Merck Index
HSDB & RTECS Database
RxList Monographs

MSDS:

U.S. Pharamacopeia

Validation date: (year.month)

March 6, 2008

Revision date: 9/7/2011.

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