

1PHARMACIA

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**** MATERIAL SAFETY DATA SHEET ****

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

COMMON NAME: STREPTOZOCIN
SYNONYMS: 18883-66-4 - CAS NUMBER
175400 - EDP NUMBER
481470 - EDP NUMBER
PNU-9889 - PHARMACIA & UPJOHN PNU#
MOLECULAR FORMULA: C8-H15-N3-O7
CHEMICAL FAMILY: Antibiotic
USE: Antineoplastic drug
MANUFACTURER/SUPPLIER: PHARMACIA & UPJOHN CO., A SUBSIDIARY OF
PHARMACIA CORP.
7171 PORTAGE RD
KALAMAZOO, MI 49001-0199

DATA SOURCE: PHARMACIA & UPJOHN CO., A SUBSIDIARY OF
PHARMACIA CORP.
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KALAMAZOO, MI 49001-0199

TELEPHONE NUMBERS: (269) 833-5122 - (24 HOURS)
(269) 833-7555 - (8:00 a.m. - 4:30 p.m.)
(269) 833-2358 - (SAMPLE REQUEST/TECHNICAL ASSISTANCE)

2. COMPOSITION/INFORMATION ON INGREDIENTS

INGREDIENT 1
COMMON NAME: Streptozocin
% BY WEIGHT: 100 %
CAS NUMBER: 18883-66-4
EXPOSURE LIMIT(S): Not established.

3. HAZARDS IDENTIFICATION

EFFECTS OF OVEREXPOSURE: The most common toxic effect to occur from streptozocin is renal (kidney) toxicity. Such toxicity is dose-related and cumulative and may be severe or fatal. Other major toxicities are nausea and vomiting and alterations in liver function. Streptozocin may affect glucose metabolism. A diabetic effect has been reported. Effects of the blood are rare but some toxicity has been observed. Streptozocin is an irritant to tissues and may lead to local ulceration and necrosis. Streptozocin is mutagenic in bacteria, plants, and mammalian cells. It has been shown to be carcinogenic in mice. Animal studies show streptozocin to be a teratogen and cause adverse effects on fertility. Eyes: may cause irritation. Skin: may cause severe irritation. Inhalation: no information found.
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Not established.

4. FIRST AID MEASURES

EYES: Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes.

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SKIN: Wash with soap and water for 15 minutes.
INHALATION: Move to fresh air.
INGESTION: Contact a physician or poison control center.

5. FIRE FIGHTING MEASURES

FLASH POINT: Not applicable. (solid)
LOWER EXPLOSION LIMIT (LEL): Not applicable.
UPPER EXPLOSION LIMIT (UEL): Not applicable.
EXTINGUISHING MEDIA: Water, carbon dioxide, or dry chemical.
FIRE-FIGHTING PROCEDURES: Wear self-contained breathing apparatus and full body protective equipment.
UNUSUAL FIRE OR EXPLOSION HAZARDS: As with all finely divided organic powders, it is advisable to eliminate explosion hazards by methods such as grounding mechanical equipment in contact with the material to prevent the buildup of static electricity, inerting the atmosphere or controlling dust levels.
HAZARDOUS COMBUSTION PRODUCTS: Carbon monoxide and nitrogen oxides.

6. ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED: Small spills washed to drain with water. Large spills (over 5 gallons) should be contained to prevent entering drains or storm sewers. Degradation by strong alkali very rapid, but generates diazomethane.

7. HANDLING AND STORAGE

PRECAUTIONS FOR HANDLING AND STORING: Avoid generating dust and contact with skin, eyes and clothing. Wash thoroughly after handling. Launder contaminated clothing before reuse. Store at room temperature. Protect from light.
PRODUCT PREPARATION AND ADMINISTRATION: Hospital personnel preparing or administering parenteral antineoplastic agents should wear latex or surgical rubber gloves, safety glasses, a closed-front gown with knit cuffs and masks. Preparation of all antineoplastic agents should be done in a class II laminar flow biological safety cabinet with exhaust air discharged external to the room environment. All needles, syringes, vials, ampules and other equipment or disposable clothing which have been in contact with antineoplastic agents should be segregated and incinerated at a temperature not less than 1000 degrees centigrade. Sealed containers should be opened prior to incineration.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

RESPIRATORY PROTECTION: Approved respirator where the potential for airborne exposure exists.
VENTILATION: Local exhaust at point of manufacture or use.
PROTECTIVE GLOVES: Rubber.
EYE PROTECTION: Safety glasses with side-shields.
OTHER PROTECTIVE EQUIPMENT: Protective covering for exposed areas of skin.

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE/PHYSICAL STATE: Ivory-colored crystalline powder

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BOILING POINT: Not applicable.
EVAPORATION RATE: Not applicable.
FREEZING POINT: No information found
MELTING POINT: 115 C (239 F) (decomposes)
MOLECULAR WEIGHT: 265.22
ODOR: No information found
PARTITION COEFFICIENT (n-OCTANOL/WATER): 2.704 (log P estimate)
PH: No information found
SOLUBILITY IN SOLVENTS: Alcohols and ketones
SOLUBILITY IN WATER: Soluble
SPECIFIC GRAVITY (WATER=1): No information found
VAPOR DENSITY (air = 1): Negligible
VAPOR PRESSURE: Negligible
VOLATILITY: Negligible

10. STABILITY AND REACTIVITY

STABILITY: Bulk drug is stable for 25 months when stored in a cool room with double plastic bags and fiber drums; formulated product is stable for 2 years when stored in the refrigerator. The recommended controlled room storage temperature is 4 degrees centigrade. The possibility of light sensitivity of the bulk drug and the product has been suggested by recent studies; therefore caution should be taken during production and manufacturing to shield the bulk drug from light.

INCOMPATIBILITY WITH OTHER MATERIALS: None.

HAZARDOUS POLYMERIZATION: The drug is characterized by a strong exotherm beginning at 108 degrees centigrade. The gas which is evolved accounts for approximately 38% of the sample. The heat given off during thermal decomposition indicates that the powder should be stored at temperatures no higher than controlled room temperature (recommended 4 C) since the first trace of decomposition would quickly raise the temperatures of the material, resulting in "runaway" decomposition. There are obvious potential risks associated with streptozocin if it is improperly stored or sent to disposal. If proper storage and disposal requirements for this material are met, the potential risks during production and manufacture are minimal.

11. TOXICOLOGICAL INFORMATION

ACUTE STUDIES:

SENSITIZATION: No information found.
INTRAVENOUS LD50 (DOG): 25 - 50 MG/KG
INTRAVENOUS LD50 (RAT): 108 - 176 MG/KG
INTRAVENOUS LD50 (MOUSE): 274.8 MG/KG
ORAL LD50 (RAT): 5,150 MG/KG
ORAL LD50 (MOUSE): > 3,000 MG/KG
INTRAPERITONEAL LD50 (MOUSE): 219 MG/KG
SUBCUTANEOUS LD50 (MOUSE): 335 MG/KG

OTHER STUDIES:

GENOTOXICITY:
Mutagenicity: salmonella typhimurium: mutagenic.
Mammalian cell mutation: mutagenic.
TERATOGENICITY: Studies of animals show developmental abnormalities and effects on fertility.

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CARCINOGENICITY:

Listed by NTP as reasonably anticipated to be a carcinogen. Listed by IARC as possibly carcinogenic to humans (2B).
IV and IP (rat): carcinogenic.
Oral and topical (rat): carcinogenic.

12. ECOLOGICAL INFORMATION

ENVIRONMENTAL FATE:

MOBILITY: Streptozocin melts at 115 C. It has no measurable vapor pressure and negligible volatility, therefore it is not expected to enter the air. Because of its estimated low octanol water partition coefficient (log P estimate -2.704) it would not be expected to sorb to most organic soils. Streptozocin is soluble in water and would be expected to be relatively mobile and migrate toward the aquatic compartment.

PERSISTENCE/DEGRADABILITY: No information found.

BIOACCUMULATIVE POTENTIAL: Streptozocin has a low octanol water partition coefficient (-2.704) and would be expected to have a low bioaccumulative potential.

ABIOTIC POTENTIAL: Streptozocin, as with all antibiotics, may have some initial inhibitory effects on the most sensitive microorganisms until it is degraded.

ECOTOXICITY: No information found.

13. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL METHOD: Incinerate according to local, state and federal regulations at 1,000 degrees C or greater. Streptozocin is listed under the Resource Recovery and Conservation Act (RCRA) as a hazardous waste (U206). Streptozocin can be safely deactivated by a reaction with sulfamic acid. The procedure is as follows: 1. Inject 3 ml sulfamic acid solution (0.5 gm sulfamic acid/3 ml) into the vial. 2. Vent vial by leaving needle in vial. 3. Swirl vial to dissolve material (nitrogen gas evolves immediately). 4. Let stand approximately 16 hours.

14. SHIPPING REGULATIONS

PROPER SHIPPING NAME: Environmentally hazardous substances, solid N.O.S. (streptozocin).

HAZARD CLASS: 9.

SUBSIDIARY RISK: None.

UN/NA NUMBER: UN3077.

PACKING GROUP: III.

EMERGENCY RESPONSE GUIDE: 31.

IMDG CODE PAGE: 9028.

TRANSPORTATION LABELS: Class 9.

REPORTABLE QUANTITY: 0.454 KG

SPECIAL PROVISIONS: 8, B54.

This material is only regulated when the quantity per package is equal to or exceeds the CERCLA reportable quantity listed in Appendix A to 49CFR 172.101.

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15. OTHER INFORMATION

REVIEWED BY: Environment and Safety.

DISCLAIMER: The information contained in the MSDS is believed to be correct as of its date of issuance. BY MAKING THE MSDS AVAILABLE, PHARMACIA & UPJOHN CO. DOES NOT MAKE ANY EXPRESS OR IMPLIED WARRANTY (INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE) REGARDING THE MSDS, ITS ACCURACY OR THE PRODUCT TO WHICH IT RELATES. Anyone using this information agrees that Pharmacia & Upjohn shall not be held liable (based on its negligence or otherwise) for any personal injury or other damage relating to, or arising from such use, including direct, incidental, or consequential damage and such user agrees to indemnify Pharmacia & Upjohn for any claims arising out of its use.

16. LABELING

PHARMACIA & UPJOHN PRECAUTIONARY LABEL CODE(S): M, N-1

HAZARD: REPRODUCTIVE HAZARD. CARCINOGEN.

SIGNAL WORD: DANGER!

STATEMENT OF HAZARD/RISK PHRASE: May cause adverse reproductive effects in males and/or females. This material may cause cancer in animals and/or humans

PRECAUTIONARY MEASURES: Avoid exposure. Do not get in eyes, on skin, on clothing. Do not breathe dust, vapor, mist or gas. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling.