



TEVA PARENTERAL MEDICINES

Material Safety Data Sheet

Cisplatin Injection, USP

1. PRODUCT IDENTIFICATION

Product Name Cisplatin Injection, USP
Product Use Medical Treatment; Antineoplastic Agent
Manufacturer Teva Parenteral Medicines, Inc.
Address 11 Hughes
 Irvine, CA 92618-1902

Chemtrec Emergency No. 1-800-424-9300 (United States)
 1-202-483-7617 (International Collect)
Business Phone 1-800-729-9991
Website Address <http://www.newsicor.com>

Common Names Platinol®-AQ
Chemical Name cis-Platinous Diammine Dichloride
Chemical Formula Pt (NH₃)₂Cl₂
Chemical Family Heavy metal complex
How Supplied 50 mg in 50 mL vial (1 mg/mL)
 100 mg in 100 mL vial (1mg/mL)

Date of Preparation: December 4, 2005

2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	EXPOSURE LIMITS IN AIR					
		Wt%	ACGIH		OSHA		Other
			TLV	CEIL	PEL	CEIL	
Cisplatin (exposure limit for Platinum, soluble salts as Platinum)	15663-27-1	0.1	0.002 mg/m3	NE	0.002 mg/m3	NE	0.002 mg/m3*
Sodium Chloride	7647-14-5	0.9	NE	NE	NE	NE	NE
Water (for injection)	7732-18-5	99	NE	NE	NE	NE	NE

NE – Not Established C – Ceiling Limit *NIOSH REL

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 format

CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

3. HAZARD IDENTIFICATION

EMERGENCY OVERVIEW: Material is a clear, slight yellow liquid. It is a cytotoxic agent and a probable cancer hazard. Highly toxic if injected or swallowed. Eye and skin irritant. May cause damage to the reproductive system, kidneys, blood, hearing and nervous system. Harmful to the fetus. May cause allergic skin and/or respiratory reactions. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Do not taste or swallow. Wash thoroughly after handling.

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3. HAZARD IDENTIFICATION cont.-

Symptoms of Overexposure by Route of Exposure: This material is intended for injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness swelling and damage to the eyes and redness, itching burning and damage to the skin. May cause allergic skin reactions.

Ingestion: Ingestion is not an anticipated route of occupational exposure. However, the active ingredient, Cisplatin, is highly toxic if swallowed. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including decreased blood platelets and white blood cells, nausea, vomiting, diarrhea, anemia, skin rash, tinnitus, hearing loss, electrolyte disturbances, irritation of the respiratory tract and hemolysis may occur. Severe injection overexposure may be fatal. See package insert for other adverse reactions associated with therapeutic doses of this product.

Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as decreased blood platelets and white blood cells, nausea, vomiting, diarrhea, anemia, skin rash, tinnitus, hearing loss, electrolyte disturbances, irritation of the respiratory tract and hemolysis may occur.

Cancer: Cisplatin is considered probably carcinogenic (see Section 11).

Chronic: Cisplatin, is considered a potential reproductive and developmental toxicant (see Section 11).

Target Organs: Potential hazard to the kidneys, blood, hearing and nervous system (see Section 11).

Pre-Existing Medical Conditions: Pre-existing kidney, blood, hearing and nervous system disorders may be aggravated by exposure to this material.



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6. ACCIDENTAL RELEASE MEASURES

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

7. HANDLING and STORAGE

CISPLATIN IS A CYTOTOXIC AGENT. ALL WORK PRACTICES MUST BE DESIGNED TO REDUCE HUMAN EXPOSURE TO THE LOWEST LEVEL.

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from sources of ignition and any incompatible materials or conditions (see Section 10). Store at room temperature 15-25°C (59-77°F). Protect from light. Do not use discolored solutions.

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.



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8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 100 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances where air-purifying respirators may not provide adequate protection. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: A full body gown which is closed at the front and has long sleeves is recommended.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	ND	Evaporation Rate (n-BuAc=1):	ND
Specific Gravity (water = 1):	ND	Melting/Freezing Point:	0°C (32°F)
Solubility in Water:	Sparingly	Boiling Point:	100°C (212°F)
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	5-7 (1% solution)
Odor Threshold: ND			
Appearance and Color: Clear, colorless to straw colored solution, free of visible particles			

ND = No Data

10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility. Contact with aluminum may lead to the formation of a platinum precipitate.

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Oxides of carbon and nitrogen and platinum-containing compounds with possible carcinogenic potential.



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11. TOXICOLOGICAL INFORMATION

Toxicity Data: The following information is for Cisplatin, the active ingredient

Oral LD50(rat) = 25.8 mg/kg	Oral LD50(mouse) = 32.7 mg/kg
IP LD50 (mouse) = 6.6 mg/kg	Subcutaneous LD50(rat) = 8.1 mg/kg
IV LD50 (rat) = 8 mg/kg	Subcutaneous LD50(mouse) = 13 mg/kg
IP LD50(rat) = 6.4 mg/kg	IP LD50(mouse) = 13.5 mg/kg
IM LD50 (rat) = 9.2 mg/kg	IV LD50 (mouse) = 11 mg/kg
IM LD50 (mouse) = 17.9 mg/kg	IP LD50 (g. pig) = 9.7 mg/kg

Suspected Cancer Agent: Multiple intraperitoneal administrations of cisplatin to mice significantly increased the incidence and number of lung adenomas. Similar treatments caused a significant increase in the incidence of skin papillomas in mice given promoting treatment of croton oil applied to the skin. The incidences of epidermoid carcinomas and of both malignant and benign tumours in internal organs were increased by the same treatment, but were not significantly different from those in controls. In two studies, multiple intraperitoneal injections of cisplatin to rats induced leukemia. It is listed as carcinogenic by NTP, IARC and OSHA.

Irritancy of Product: This product is expected to be irritating to contaminated skin, eyes and other tissues.

Sensitization to the Product: Considered to be an allergen based on platinum compounds.

Target Organ(s): Based on studies of patients administered the drug may include nephrotoxicity (effects on the kidney), ototoxicity (effects on the ears, including ringing in the ears), and hematologic/blood effects (decreased platelets and leukocytes).

Reproductive Toxicity Information: Listed below is information concerning the effects of Cisplatin on human and animal reproductive systems. This material is classified as a Pregnancy Category D (Positive evidence of risk). Currently, there have been no studies in pregnant women.

Mutagenicity: In general, studies have produced positive (genotoxic) results. Cisplatin induced structural chromosomal aberrations and sister chromatid exchanges in cells of rodents treated *in vivo*, but it did not induce dominant lethal mutations in mice. It transformed Syrian hamster embryo cells; it induced chromosomal aberrations, micronuclei and sister chromatid exchanges in both human and rodent cells *in vitro*, and mutation and DNA damage (including DNA cross-links) in rodent cells *in vitro*. In *Drosophila*, cisplatin induced aneuploidy and dominant lethal and sex-linked recessive lethal mutations. It induced chromosomal aberrations and mutation in plants. Cisplatin induced mutation, gene conversion and DNA damage in fungi and mutation and DNA damage in bacteria.

Embryotoxicity/Teratogenicity: In most animal experiments, cisplatin caused an increase in embryoletality but teratogenic effects were not seen.

Reproductive Toxicity: In men, the use of cisplatin in the chemotherapy of testicular tumors is frequently associated with decreased spermatogenesis and abnormal Leydig cell function. Similar findings have also been reported in experimental animal studies. Sperm production has been observed to return to normal levels in 50 to 60% of treated men between 1 and 3 years after chemotherapy is discontinued. Although fertility is apparently reduced, it is still possible for these patients to father children.

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11. TOXICOLOGICAL INFORMATION cont...

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

12. ECOLOGICAL INFORMATION

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: It is anticipated that this compound will decompose into a variety of organic compounds.

Effect of Materials on Plants or Animals: This product may be harmful to contaminated plant and animal life. See Section 11 (Toxicological Information) for additional information.

Effect of Chemicals on Aquatic Life: This product may be harmful to aquatic plant and animal life in contaminated bodies of water, especially if released in large quantities.

13. DISPOSAL CONSIDERATIONS

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA "listed" or "characteristic" hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

14. TRANSPORTATION INFORMATION

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable



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15. REGULATORY INFORMATION

U.S. REGULATIONS

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. TSCA Inventory Status: Cisplatin is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product contains a chemical known to the State of California to cause cancer - Cisplatin.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne pathogen Standard (29 CFR 1910.1030) are applicable.

CANADIAN REGULATIONS

Canadian DSL/NDSL Status: Cisplatin is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): DANGER! Cytotoxic Agent. Accidental Injection or Ingestion Can Be Fatal. Highly toxic if injected or swallowed. Eye and skin irritant. May cause damage to the reproductive system, kidneys, blood, hearing and nervous system. Harmful to the fetus. May cause allergic skin and/or respiratory reactions. Avoid contact with eyes, skin and clothing. Avoid exposure during pregnancy and while breastfeeding. Do not taste or swallow. Wash thoroughly after handling. Cisplatin should be administered under the supervision of a qualified physician. Avoid accidental injection. Do not eat, drink or smoke when handling Cisplatin. Clean up spills promptly.

16. OTHER INFORMATION

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The information in this document is believed to be correct as of the date issued. **HOWEVER, NO WARRANTY OF MERCHANTABILITY, FITNESS FOR ANY PARTICULAR PURPOSE, OR ANY OTHER WARRANTY IS EXPRESSED OR IS TO BE IMPLIED REGARDING THE ACCURACY OR COMPLETENESS OF THIS INFORMATION, THE RESULTS TO BE OBTAINED FROM THE USE OF THIS INFORMATION OR THE PRODUCT, THE SAFETY OF THIS PRODUCT, OR THE HAZARDS RELATED TO ITS USE.** This information and product are furnished on the condition that the person receiving them shall make his own determination as to the suitability of the product for his particular purpose and on the condition that he assume the risk of his use thereof.