



Bristol-Myers Squibb Company

MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

BRISTOL-MYERS SQUIBB WORLDWIDE MEDICINES GROUP
 P.O. BOX 191
 NEW BRUNSWICK, NJ 08903
 732-519-3683

November 20, 2000

Product Identification Platinol

Chemical Name: Cis-Diamminedichloroplatinum
 Synonym: Cisplatin; BMY 25936
 How Supplied: White lyophilized powder (10 or 50 mg cisplatin/vial, as labeled)
 Product Use: Platinol contains cisplatin, and is used to treat certain neoplastic diseases.
 Chemical Family: Heavy metal complex
 Molecular Formula: C12H6N2Pt CAS NUMBER: 15663-27-1

EMERGENCY CONTACTS

Transportation: CHEMTREC (800)424-9300. For all international transportation emergencies call Chemtrec at (703)527-3887, collect call accepted.

EMERGENCY OVERVIEW: Platinol is a white lyophilized powder which is packaged in vials. This formulation contains cisplatin, a potent cytotoxic drug. Cisplatin is highly toxic after acute ingestion. Mutagen. Potential carcinogen. Teratogen. Possible reproductive effector.

2. COMPOSITION/ INFORMATION ON INGREDIENTS

COMPONENTS	HAZARDOUS (Y/N)	CONCENTRATION (wt %)	CAS NUMBER	EXPOSURE GUIDELINE
Cisplatin	Y	5	15663-27-1	2 ug/m3 (for platinum) (1)
Mannitol	N	>1	69-65-8	none
Sodium Chloride	Y	>1	7647-14-5	none
Hydrochloric Acid used for pH adjustment			7647-01-0	

1 OSHA PEL = Occupational Safety and Health administration - Permissible Exposure Limit

3. HEALTH HAZARDS IDENTIFICATION

EFFECTS OF OVEREXPOSURE

Routes of Entry:

1. Inhalation: Under normal conditions, this product is contained within vials and inhalation would not be expected to occur. However, if material becomes airborne there is potential for inhalation. The extent of systemic absorption of cisplatin after inhalation is unknown.



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

2. Skin Contact: Under normal conditions, this product is contained within vials and skin contact would not be expected to occur. Exposure to cisplatin may occur via skin contact if the vials break or spill and if gloves and protective clothing are not worn. The extent of systemic absorption of cisplatin after skin contact is not known.

3. Ingestion: Ingestion of large quantities of this material in an occupational setting would not be expected to occur. Ingestion of trace amount of the material might occur if vials are broken or spilled, if material contacts hands and if hands are not washed prior to eating, drinking, or smoking. The extent of systemic absorption of cisplatin from the gastrointestinal tract is not known.

Acute

Ingestion: Platinol contains cisplatin, a potent cytotoxic drug. In animals cisplatin is highly toxic after acute ingestion. Since it is not administered orally for therapeutic use there is no information in humans concerning signs after exposure via this route. See also "Other."

Inhalation: There is no information concerning the potential of this material to produce symptoms after inhalation. Transient bronchial irritation may occur.

Skin Contact:

a. Toxic: There is no information concerning the potential of this material to produce symptoms after skin contact.

b. Irritation: The irritation potential of this material has not been evaluated. However, Platinol contains irritant substances. Therefore, if a vial is opened and skin contact occurs, the potential for mild irritation exists, however moderate or severe irritation is not expected.

c. Sensitization: This material may produce a possible rash upon contact.

Eye Contact: This material may cause conjunctivitis.

Other: Platinol is intended for intravenous injection under the supervision of physicians experienced in cancer chemotherapy. Cisplatin is highly toxic after acute intravenous exposure. Nausea and vomiting occur in almost all patients receiving this drug. Anaphylactoid reactions, consisting principally of facial edema, flushing, wheezing or respiratory difficulty, tachycardia, and hypotension, have occurred in some patients receiving the drug.

Chronic: Cisplatin is a potent cytotoxic drug that is administered intravenously. Side effects reported in persons treated with therapeutic doses of this drug include dose-related: kidney toxicity and electrolyte disturbances; ototoxicity (e.g. ringing of the ears and/or hearing loss); peripheral neuropathy; and moderate and reversible hematologic (blood) effects. Non-dose-dependent adverse effects include: nausea and vomiting; and anaphylactoid reactions. Cisplatin is a mutagen and a possible carcinogen.

Exposure Guideline Summary: Exposure guideline not established.

Carcinogen Lists IARC: Yes NTP: Yes OSHA: No
Cisplatin has been classified in Group 2A by IARC and as "reasonably anticipated to be a carcinogen" by NTP. A 2A designation indicates that IARC



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

believes cisplatin to be a probable human carcinogen, although there is limited human evidence. However, sufficient evidence of carcinogenicity in laboratory animals exists: cisplatin administration has been associated with lung adenomas and skin papillomas in mice, and leukemia in rats.

Target Organs: The kidneys, nervous system, hematopoietic system, and gastrointestinal system are the major target organs. Other organ systems which undergo rapid cellular division may also be targets after systemic exposure.

Medical Conditions Aggravated by Exposure: Therapeutic doses of this material may aggravate kidney disease, hearing disorders, neurological diseases, and anemia or other forms of bone marrow suppression.

Medical Surveillance Recommendation: A pre-placement physical examination and history (noting any risk factors) for employees with potential exposure to Platinol is recommended. A complete blood count, including differential, test(s) of renal function, urine analysis and hearing test may be taken to provide a baseline. Periodic follow-up examinations should be given in accordance with institutional policy, overseen by a physician thoroughly knowledgeable about both the toxicity of the substance and the extent of work place exposure. A permanent registry of all staff who routinely prepare or administer Platinol should be considered. Staff members who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring workers' health.

FOR MORE INFORMATION REFER TO SECTION 11: TOXICOLOGICAL INFORMATION

4. FIRST AID MEASURES

Ingestion: Seek medical attention immediately. Induction of vomiting should be considered for significant ingestion if person is conscious and not experiencing convulsions. Never give anything by mouth to an unconscious person.

Inhalation: Remove exposed person to fresh air. If person is not breathing give artificial respiration. If breathing is difficult administer oxygen. Get medical attention.

Skin Contact: Immediately flush with large amounts of water. Use soap if available. Remove contaminated clothing, including shoes after flushing has begun. Get medical attention.

Eye Contact: Hold eyelids apart and flush with running water for at least 15 minutes. Get medical attention immediately.

Note to physicians: Product contains a potent cytotoxic antineoplastic drug.

5. FIRE FIGHTING MEASURES

Flash point: Not determined.

Autoignition Temperature: Not determined.

Flammability limits

LEL: Not determined.

UEL: Not determined.



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FIRST AID MEASURES (CONTINUED)

Combustibility of Dusts: Fine powders are considered to be combustible. Provide appropriate bonding and grounding protection to control static charges. Powder handling systems such as dust collectors, dryers, and mills may require additional protective measures (ie. explosion venting).

Extinguishing Media: Unlikely to burn in vial. In case of fire, flood with water.

Firefighting Instructions: Firefighters should wear self contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Evacuate personnel to upwind direction, remove unneeded material and cool container(s) with water from a maximum distance.

Hazardous Combustion Products: CO, CO_x, HCl, NO_x, and possibly other compounds with carcinogenic potential.

Unusual Hazards: Product contains a potent cytotoxic drug. Avoid inhalation, ingestion, skin contact. Decontaminate protective equipment after use.

6. ACCIDENTAL RELEASE MEASURES

Spill/Clean-up: Small spills -- wipe liquids with absorbent gauze pads. Clean using detergent and water. If powder spills cover with gauze pads or paper towel. Soak with water and wipe up. Clean area thoroughly using detergent and water.

Large spills -- cover liquid with absorbent sheets, spill-control pads or pillows. Clean using detergents and water. Refer to WHO monograph (IARC Scientific Publication number 73) for details on chemical deactivation. Treat product and contaminated materials as hazardous material. Incineration is recommended.

7. HANDLING AND STORAGE

Handling Precautions: Do not break vials or spill contents. See relevant guidance for handling of cytotoxic materials.

Container Requirements: Do not allow Platinol to contact aluminum. Aluminum reacts with formulated Platinol, causing precipitate formation and a loss of potency.

Storage Conditions: Should be stored at room temperature (15-25 degrees C). Do not refrigerate. Protect from light.

8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

Ventilation Requirements: Local mechanical exhaust ventilation recommended to minimize employee exposure. Control exposure by enclosure to processes whenever possible. A biological safety cabinet (BSC) should be used for preparation of this drug, or as determined appropriate by industrial hygienist.

Respiratory Protection: When engineering controls are not sufficient to control exposure, or if BSC is not available, wear approved respirator with high efficiency dust filter, or powered air-purifying respirator; self-contained breathing apparatus should be available for emergency use.



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EXPOSURE CONTROLS AND PERSONAL PROTECTION (CONTINUED)

Eye Protection: Wear chemical safety goggles (ANSI Z87.1).

Protective Gloves: Wear disposable surgical latex gloves rather than polyvinyl chloride (PVC) gloves. Gloves should be changed regularly and removed immediately after overt contamination. Double gloving is recommended for cleaning up spills.

Special Clothing: Wear impervious disposable coveralls with closed front, long sleeves and elastic cuffs, and boots to protect from dusts, splashes, or sprays. Remove disposable clothing prior to leaving the work area.

Hygiene: Wash hands, forearms, and face thoroughly after handling compounds and before eating, smoking, using lavatory, and at the end of day.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance/Physical State/Color: White lyophilized powder which is packaged in vials.

Boiling point: Not applicable.

Evaporation rate: Not applicable.

Flash point: Not determined.

Freezing point: Not applicable.

Melting point: 270 degrees C

Octanol/water partition coefficient: Not determined.

Odor (threshold): Unknown

pH: 3.5-5.5 (reconstituted solutions)

Solubility in water: 1 mg/ml (solubility in dimethylformamide = 24 mg/ml)

Specific gravity: Not determined.

Vapor density: Not applicable.

Vapor Pressure: Not determined.

Viscosity: Not applicable.

10. STABILITY AND REACTIVITY

Stability: When stored at room temperature (15-25 degrees C) in original container, material is stable to expiration date shown on product label.

Incompatibilities: No known hazardous incompatibilities. An unusual incompatibility is the formation of a platinum precipitate when Platinol comes in contact with aluminum.

Conditions of Reactivity: No information.

Hazardous Decomposition Products: CO, CO_x, HCl, NO_x, and possibly other compounds with carcinogenic potential.



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STABILITY AND REACTIVITY (CONTINUED)

Hazardous Polymerization: Will not occur in original container to expiration date.

Explosion data relative to mechanical impact: No information.

Explosion data relative to static discharge: No information.

11. TOXICOLOGICAL INFORMATION (for cisplatin)

RTECS NUMBER (U.S.): TP2450000

ACUTE

LD 50:

Acute oral LD50 (rat) = 25.8 mg/kg;
Acute oral LD50 (mouse) = 32.7 mg/kg;
Acute oral LD50 (mouse) = 52.6 mg/kg;
Acute iv LD50 (rat) = 8 mg/kg;
Acute iv LD50 (mouse) = 11 mg/kg;
Acute ip LD50 (rat) = 7 mg/kg;
Acute ip LD50 (mouse) = 8.6 mg/kg;
Acute ip LD50 (guinea pig) = 9.7 mg/kg;
Acute im LD50 (rat) = 9.2 mg/kg;
Acute im LD50 (mouse) = 17.9 mg/kg;
Acute sc LD50 (rat) = 8.1 mg/kg;
Acute sc LD50 (mouse) = 13 mg/kg.

LC 50: Not tested.

LD 50: (formulated product)
Acute oral LD50 (rat) = 500 mg/kg.

CHRONIC

Carcinogenicity: Cisplatin has been shown to be carcinogenic in mice and rats. The drug should be considered a potential carcinogen in humans.

Mutagenicity: Cisplatin was positive in a battery of genetic toxicity tests. It has been shown to be mutagenic in bacteria and has produced chromosomal aberrations in animals cells in culture.

Teratogenicity: Cisplatin may cause fetal harm when administered to pregnant women. Cisplatin has been shown to be teratogenic in mice and embryotoxic in mice and rats.

Reproductive Effects: The effects of cisplatin on the gonads and fertility have not been fully determined. Since the drug has produced testicular atrophy in animals and platinum is distributed in high concentration into testes, a risk of adverse testicular effects in humans may exist.

Toxicological synergistic products: Therapeutic use of Cisplatin produces cumulative kidney toxicity that is potentiated by aminoglycoside antibiotics. Cisplatin may potentiate the ototoxic effects of other drugs, such as ethacrynic acid.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information: Not determined.

Chemical Fate Information: Not determined.



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13. DISPOSAL CONSIDERATIONS

Disposal: Dispose of in accordance with national, state, local or applicable country regulations. Treat products and contaminated materials as hazardous material. Incineration at an approved facility is recommended.

14. TRANSPORT INFORMATION

DOMESTIC

Hazard Class (UN NUMBER): Not regulated by D.O.T.
Proper shipping name: Not applicable.
Label requirements: Not applicable.
Placard requirements: Not applicable.
Limited Quantity Exemption: Not applicable.

INTERNATIONAL

Hazard Class (UN NUMBER or PIN NUMBER): Not regulated.
Proper shipping name: Not applicable.
Label requirements: Not applicable.
Placard requirements: Not applicable.
Limited Quantity Exemption: Not applicable.

15. REGULATORY/STATUTORY INFORMATION -- not meant to be all inclusive

U.S. Federal: None noted.

International: None noted.

EC Labeling: None noted.

California: Product contains cisplatin which is subject to California Proposition 65 carcinogen warning and release requirements.

16. OTHER INFORMATION

November 20, This MSDS was revised to change telephone numbers.

Federal law prohibits dispensing without prescription. See package insert for recommended medical use. See OSHA Instruction PUB 8-1.1 for additional work practice guidelines for handling this material. Copies are available from OSHA Room N3651, 200 Constitution Ave., NW, Washington, DC 20210.

Therapeutic agents are intended for use under direction of a physician and/or under the conditions of use described on the label. As a general precaution, personnel who handle drug substances should avoid contact (ingestion, inhalation, skin and eye contact) with these substances.

This material safety data sheet is intended for use by personnel who handle this material as part of their job responsibilities. It does not address the therapeutic use of this material. Information concerning the therapeutic use of this drug substance should be obtained from formulated product package inserts and other appropriate references.

The information contained in this MSDS is believed to be accurate and represents the best information available at the time of preparation. However, we make no warranty, express or implied, with respect to such information, and we assume no liability from its use.