



PHARMACY MEDICINE
KEEP OUT OF REACH OF CHILDREN

Rx Only

Cisplatin 1mg/1ml Injection BP

STERILE SOLUTION FOR SINGLE DOSE INTRAVENOUS INFUSION USE ONLY

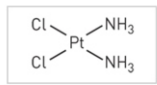
Rx only

COMPOSITION

Table with 2 columns: Component and Quantity. Includes CISPLATIN 10, Cisplatin Injection BP 10 mg/10 mL, and Cisplatin BP 1 mg.

DESCRIPTION

CISPLATIN (Cisplatin Injection) is a clear colorless sterile aqueous solution, available in 10 and 50 mL multiple dose vials, each mL containing 1 mg cisplatin 9 mg sodium chloride in water for injection.



Cis-diamminedichloroplatinum (II) (Cisplatin)

CLINICAL PHARMACOLOGY

Plasma concentrations of parent compound, cisplatin, decay monoexponentially with a half-life of about 20 to 30 minutes following bolus administration of 50 or 100 mg/m2 doses.

patients respond differently than younger patients. In four clinical trials of combination chemotherapy for advanced ovarian carcinoma, 1484 patients received cisplatin either in combination with cyclophosphamide or paclitaxel.

ADVERSE REACTIONS

Nephrotoxicity - Dose related and cumulative renal insufficiency is the major dose-limiting toxicity of cis-platin. Renal toxicity has been noted in 28% to 36% of patients treated with a single dose of 50 mg/m2.

Ototoxicity- Ototoxicity has been observed in up to 31% of patients treated with a single dose of cisplatin 50 mg/m2, and is manifested by tinnitus and/or hearing loss in the high frequency range (4,000 to 8,000Hz).

Hematologic- Myelosuppression occurs in 25% to 30% of patients treated with cisplatin. The nadirs in circulating platelets and leukocytes occur between days 18 to 23 (range 7.5 to 45) with most patients recovering by day 39 (range 13 to 62).

sulfhydryl groups of amino acids or proteins, accounts for the instability of cisplatin in biological matrices. The ratios of cisplatin to total free (ultra filterable) platinum in the plasma vary considerably between patients and range from 0.5 to 1.1 after a dose of 100 mg/m2.

Following cisplatin doses of 20 to 120 mg/m2, the concentrations of platinum are highest in liver, prostate, and kidney, somewhat lower in bladder, muscle, testicle, pancreas, and spleen and lowest in bowel, adrenal, heart, lung, cerebrum, and cerebellum.

Over ac dose rang of 40 to 140 mg cisplatin/m2 given a bolus injection or as infusions varying in length from 1 hour to 24 hours, from 10% to about 40% of the administered platinum is excreted in the urine in 24 hours.

INDICATIONS

CISPLATIN (Cisplatin Injection) is indicated as therapy to be employed as follows:

Metastatic Testicular Tumors- In established combination therapy with other approved chemotherapeutic agents in patients with metastatic testicular tumors who have already received appropriate surgical and/or radiotherapeutic procedures.

Metastatic Ovarian Tumors-In established combination therapy with other approved chemotherapeutic agents in patients with metastatic ovarian tumors who have already received appropriate surgical and/or radiotherapeutic procedures.

Advanced Bladder Cancer -Cisplatin is indicated as a single agent for patients with transitional cell bladder cancer which is no longer amenable to local treatments such surgery and/ or radiotherapy

frequency and with the same timing as leukopenia and thrombocytopenia. Fever and infections have also been reported in patients with neutropenia.

In addition to anemia secondary to myelosuppression, a Coombs' positive hemolytic anemia has been reported. In the presence of cisplatin hemolytic anemia, a further course of treatment may be accompanied by increased hemolysis and this risk should be weighed by the treating physician.

The development of acute leukemia coincident with the use of cisplatin has rarely been reported in humans. In these reports, cisplatin was generally given in combination with other leukemogenic agents.

Gastrointestinal—Marked nausea and vomiting occur in almost all patients treated with cisplatin, and are occasionally so severe that the drug must be discontinued. Nausea and vomiting usually begin within 1 to 4 hours after treatment and last up 24 hours.

Other Toxicities

Vascular toxicities coincident with the use of cisplatin in combination with other antineoplastic agents have been reported rarely. The events are clinically heterogeneous and may include myocardial infarction, cerebrovascular accident, thrombotic microangiopathy (HUS), or cerebral arteritis.

Serum Electrolyte Disturbances - Hypomagnesemia, hypocalcaemia, hyponatremia, hypokalemia, and hypophosphatemia have been reported to occur in patients treated with cisplatin and probably related to renal tubular damage.

Hyperuricemia - Hyperuricemia has been reported to occur at approximately the same frequency as the increases in BUN and serum creatinine.

Neurotoxicity - Neurotoxicity, usually characterized by peripheral neuropathies, has been reported. The neuropathies usually occur after prolonged therapy (4 to 7 months); however, neurologic symptoms have been reported to occur after a single dose.

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CONTRAINDICATIONS

CISPLATIN (Cisplatin Injection) is contraindicated in patients with renal preexisting renal impairment. Cisplatin should not be employed in myelosuppressed patients, or patients with hearing impairment.

CISPLATIN (Cisplatin Injection) is contraindicated in patients with a history of allergic reactions to cisplatin or other platinum containing compounds.

DOSE AND ADMINISTRATION

Note: Needles or intravenous sets containing aluminum parts that may come in contact with cisplatin should not be used for preparation or administration.

Metastatic Testicular Tumors - The usual CISPLATIN (Cisplatin Injection) dose for the treatment of testicular cancer in combination with other approved chemotherapeutic agents is 20mg/m2 IV daily for 5 days per cycle.

Metastatic Ovarian Tumors - The usual CISPLATIN (Cisplatin Injection) dose for the treatment of metastatic ovarian tumors in combination with cyclophosphamide is 75 to 100 mg/m2 IV per cycle once every four weeks (DAY 1).

The dose of cyclophosphamide when used in combination with CISPLATIN (Cisplatin Injection) is 600 mg/m2 IV once every four weeks (DAY 1).

For directions for the administration of cyclophosphamide, refer to the cyclophosphamide package insert.

As a single agent, cisplatin should be administered at a dose of 100 mg/m2 IV per cycle once every four weeks.

Advanced bladder Cancer - CISPLATIN (Cisplatin Injection) should be administered as a single agent at a dose of 50 to 70 mg/m2 IV per cycle once every 3 to 4 weeks depending on the extent of prior exposure to radiation therapy and/or prior chemotherapy.

All Patients- Pretreatment hydration with 1 to 2 liters of fluid infused for 8 to 12 hours prior to a cisplatin does is recommended. The drug is then diluted in 2 liters of 5% dextrose in 1/2 or 1/3 normal saline containing 37.5 g of mannitol, and infused over a 6- to 8- hour period.

A repeat course of cisplatin should not be given until the serum creatinine is below 1.5 mg/100mL, and/or the BUN is below 25 mg/ 100mL.

Subsequent doses of cisplatin should not be given until an audiometric analysis indicates that auditory acuity is within normal limits.

As with other potentially toxic compounds, caution should be exercised in handling the aqueous solution. Skin reactions associated with accidental exposure to cisplatin may occur.

The use of gloves is recommended. If cisplatin contacts the skin or mucosa, immediately and thoroughly wash the skin with soap and water and flush the mucosa with water.

Procedures for proper handling and disposal of anticancer drugs should be considered. Several guidelines on this subject have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

dose of cisplatin, although this is rare. Cisplatin therapy should be discontinued when the symptoms are first observed. The neuropathy, however, may progress further even after stopping treatment.

Lhermitte's sign, dorsal column myelopathy, and autonomic neuropathy have also been reported.

Muscle cramps, defined as localized, painful, involuntary skeletal muscle contractions of sudden onset and short duration, have been reported and were usually associated in patients receiving a relatively high cumulative dose of cisplatin and with a relatively advanced symptomatic stage of peripheral neuropathy.

Ocular toxicity - Optic neuritis, papilledema, and cerebral blindness have been reported infrequently in patients receiving standard recommended doses of cisplatin.

Blurred vision and altered color perception have been reported after the use of regimens with higher doses of cisplatin or greater dose frequencies than those recommended in the package insert.

Anaphylactic-like Reactions - Anaphylactic - like reactions have been occasionally reported in patients previously exposed to cisplatin. The reactions consist of facial edema, wheezing, tachycardia, and hypotension within a few minutes of drug administration.

Hepatotoxicity - Transient elevations of liver enzymes, especially SGOT, as well as bilirubin, have been reported to be associated with cisplatin administration at the recommended doses.

Other Events - Other toxicities reported to occur infrequently are cardiac abnormalities, hiccups, elevated serum amylase, and rash.

Local soft tissue toxicity has rarely been reported following extravasation of cisplatin. Severity of the local tissue toxicity appears to be related to the concentration of the cisplatin solution.

DRUG INTERACTIONS

Plasma levels of anticonvulsant agents may become subtherapeutic during cisplatin therapy. In a randomized trial in advanced ovarian cancer, response duration was adversely affected when pyridoxine was used in combination with aletretamine (hexamethylmelamine) and cisplatin.

Caution should be exercised to prevent inadvertent overdosage with cisplatin. Acute overdosage with this drug may result in kidney failure, liver failure, deafness, ocular toxicity (including detachment of the retina), significant myelosuppression, intractable nausea and vomiting and / or neuritis.

WARNINGS

CISPLATIN (Cisplatin Injection) produces cumulative nephrotoxicity which is potentiated by aminoglycoside antibiotics. The serum creatinine, BUN, creatinine, clearance, and magnesium, sodium, potassium, and calcium levels should be measured prior to initiating therapy.

There are reports of severe neuropathies in patients in whom regimens are employed using higher doses of cisplatin or greater dose frequencies than those recommended. These neuropathies may be irreversible and are seen as paresthesias in a stocking glove distribution, areflexia, and loss of proprioception and vibratory sensation.

Anaphylactic-like reactions to cisplatin have been reported. These reactions have occurred within minutes of administration to patients with prior exposure to cisplatin, and have been alleviated by administration of epinephrine, corticosteroids, and antihistamines.

Since ototoxicity of cisplatin is cumulative, audiometric testing should be performed prior to initiating therapy and prior to each subsequent dose of drug (see ADVERSE REACTIONS section).

Cisplatin can cause fetal harm when administered to a pregnant woman. Cisplatin is mutagenic in bacteria and produces chromosome aberrations in animal cells in tissue culture.

The development of acute leukemia coincident with the use of cisplatin has rarely been reported in humans. In these reports, cisplatin was generally given in combination with other leukemogenic agents.

PRECAUTIONS

Peripheral blood counts should be monitored weekly. Liver function should be monitored periodically. Neurologic examination should also be performed regularly (see ADVERSE REACTIONS section).

Carcinogenesis, Mutagenesis, Impairment of Fertility - see WARNINGS section.

Pregnancy: Teratogenic Effects, Pregnancy Category D- see WARNINGS section.

Nursing Mothers- Cisplatin has been reported to be found in human milk; patients receiving cisplatin should not breast feed.

Pediatric Use - Safety and effectiveness in pediatric patients have not been established.

Geriatric Use -Insufficient data are available from clinical trials of cisplatin in the treatment of metastatic testicular tumors or advanced bladder cancer to determine whether elderly

after the overdosage, appears to have little effect on removing platinum from the body because of cisplatin's rapid and high degree of protein binding.

STORAGE

Store at 15° to 25°C (59° to 77°F). Do not refrigerate. Protect from light.

SHELF LIFE

24 Months

HOW SUPPLIED

CISPLATIN 10 Cisplatin Injection BP 10mg/10mL Each Sterile Single dose vial, packed in a individually carton.

CISPLATIN 50 Cisplatin Injection BP 50mg/50mL Each Sterile Multi Dose vial, packed in a individually carton.

Manufactured in India by: TAJ PHARMACEUTICALS LTD. Mumbai, India at SURVEY NO.188/1 TO 189/1,190/1 TO 4, ATHIYAWAD, DABHEL, DAMAN- 396210 (INDIA)

This leaflet was last revised in May 2019.

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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