Cisplat®

Cisplatin BP

Presentation

Cisplat®-10 concentrated solution for i.v. infusion: 1 vial of 10 ml concentrated solution for infusion contains 10 mg cisplatin BP.
Cisplat®-50 concentrated solution for i.v. infusion: 1 vial of 50 ml concentrated solution for infusion contains 50 mg cisplatin BP.

Description

Cisplatin is a heavy metal complex containing a central platinum atom surrounded by two chlorine and two ammonia molecules. Cisplatin occurs as a fine yellow powder which decomposes at 270 °C. Cisplatin is soluble in water (0.253 g/100 g at 25 °C).

Indications

Cisplatin is indicated as palliative therapy, to be employed in addition to other modalities, or in established combination therapy with other chemotherapeutic agents in the following:

- Metastatic Testicular Tumors: In patients who have already received appropriate surgical and/or radiotherapeutic and/or chemotherapeutic procedures.
- Metastatic Ovarian Tumors: As secondary therapy in patients refractory to standard chemotherapy.
- Advanced Bladder Cancer- As a single agent for patients with transitional cell bladder cancer.

Dosage And Administration

The recommended dose of Cisplatin Injection BP in adults and children as single-agent therapy is 50 to 75 mg/m^2 as a single intravenous dose every 3 to 4 weeks, or 15 to 20 mg/m^2 intravenous daily for 5 days, every 3 to 4 weeks. A repeat course of Cisplatin Injection BP should not be given until the serum creatinine is below 1.5 mg/100 mL and/or the BUN is below 25 mg/100 mL.

A repeat course should not be given until circulating blood elements are at an acceptable level (platelets ≥100,000 cells/mm^3 , WBC ≥4,000 cells/mm^2). Subsequent dose of Cisplatin Injection BP should not be given until an audiometric analysis indicates that auditory acuity is within normal limits.

When employed in combination with other antitumor drugs, the dose of Cisplatin Injection BP should be adjusted appropriately.

Pre-treatment hydration with 1 to 2 L of fluid infused for 8 to 12 hours prior to a cisplatin dose is recommended. The drug is then diluted in 2 litres 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.

Adequate hydration and urinary output must be maintained during the following 24 hours. Caution should be exercised in handling and preparing the solution of cisplatin. If cisplatin solution contacts the skin, immediately wash thoroughly with soap and water. If cisplatin solution contacts mucous membranes, flush thoroughly with water.

Reconstitution

Preparation of IV solutions:

IV needles, syringes or sets having aluminum components should not be employed in preparation or administration of Cisplatin solutions. An interaction will occur between aluminum and platinum from Cisplatin, causing a black precipitate, which is visible in the Cisplatin solution, and a loss of potency. Dilute the prepared Cisplatin Injection in 2L of 5% dextrose in one half or one third normal saline, containing 37.5 g of mannitol. Diluted Cisplatin Injection solution is suitable for intravenous infusion. This solution is not preserved; it should be used within 24 hours. Any unused portion should be discarded after that time, in order to avoid risk of microbial contamination. As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitate, discoloration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discoloration or leakage should not be used.

Contraindications

Cisplatin is contraindicated in patients with pre-existing renal impairment and hearing impairment, unless in the judgement of the physician and patient, the possible benefits of treatment outweigh the risks. Cisplatin should not be employed in myelosuppressed patients and is contraindicated in individuals who have demonstrated a previous hypersensitivity to it or other platinum-containing compounds. When used as indicated, the physician must carefully weigh the therapeutic benefit versus risk of toxicity which may occur.

Precautions

- Cisplatin should be administered under the supervision of a qualified physician experienced with the use of antineoplastic therapy.
- Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.
- Cisplatin produces cumulative nephrotoxicity which can be potentiated by aminoglycoside antibiotics.
- Serum creatinine, BUN, creatinine clearance, magnesium, sodium, potassium and calcium levels should be measured prior to initiating therapy and prior to each subsequent course.
- At the recommended dosage, cisplatin should not be given more frequently than once every 3 to 4 weeks.
- Pretreatment hydration with 1 or 2 liters of fluid infused to 8 to 12 hours prior to a cisplatin dose is recommended to minimize nephrotoxicity.
- Since ototoxicity of cisplatin is cumulative, audiometric testing should be performed prior to initiating therapy and prior to each subsequent dose of drug. Peripheral blood counts should be monitored weekly.
- Liver function should be monitored periodically. Neurologic examinations should also be performed regularly.

Adverse Reactions

Nephrotoxicity
Ototoxicity
Myelosuppression
Gastrointestinal
Serum Electrolyte Disturbances
Hyperuricemia
Neurotoxicity
Ocular Toxicity
Anaphylactic-Like Reactions
Hepatotoxicity

Drug Interactions

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

Use In Pregnancy

Cisplatin can cause fetal harm when administered to a pregnant woman. Cisplatin is mutagenic in bacteria, produces chromosome aberrations in animal cells in tissue culture and is teratogenic and embryotoxic in mice. Patients should be advised to avoid becoming pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Cisplatin has been found to have carcinogenic potential in laboratory animals. The development of acute leukemia coincident with the use of cisplatin has been reported rarely in humans. In these reports cisplatin was generally given in combination with other leukemogenic agents. As with any potent antineoplastic drug, the benefit to patient versus risk of toxicity must be carefully weighed.

Nursing Mothers

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

Overdose

Caution should be used to prevent inadvertent overdosage with Cisplatin Injection BP. 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. In addition, death can occur following overdosage. No proven antidote has been established for cisplatin overdosage. Hemodialysis, even when initiated for hours after overdosage, appears to have little effect on removing platinum from the body because of rapid and high degree of protein binding of cisplatin. Management of overdosage should include general supportive measures to sustain the patient through the period of toxicity that may occur. Patients should be monitored for 3-4 weeks in case of delayed toxicity.

Storage

Store at temperature not exceeding 25 °C in a dry place. Protect from light. Do not refrigerate.

Packaging

Cisplat®-10: Cisplatin BP (1.0 mg/ml) is supplied as a sterile preservetive free solution in 10 ml single dose glass vial, containing 10 mg of cisplatin BP.
Cisplat®-50: Cisplatin BP (1.0 mg/ml) is supplied as a sterile preservetive free solution in 50 ml single dose glass vial, containing 50 mg of cisplatin BP.

Medicine: Keep out of reach of children

For further information, please contact: 01977 158 926
(9.00 am - 5.00 pm)

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