Cistor™

Cisplatin Injection BP

DESCRIPTION

Cistor™ is a preparation of Cisplatin. Cisplatin is a heavy metal complex containing a central atom of platinum surrounded by two chloride atoms and two ammonia molecules in the cis position. Due to its unique chemical structure, the chlorine atoms of cisplatin are more subject to chemical displacement reactions by nucleophiles, such as water or sulfhydryl groups, than to enzyme-catalyzed metabolism. At physiological pH in the presence of 0.1M NaCl, the predominant molecular species are cisplatin and monohydroxymonochloro cis-diammine platinum (II) in nearly equal concentrations. The latter, combined with the possible direct displacement of the chlorine atoms by sulfhydryl groups of amino acids or proteins, accounts for the instability of cisplatin in biological matrices.

INDICATIONS

- **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. An established combination consists of Cisplatin Injection and cyclophosphamide. Cisplatin Injection, as a single agent, is indicated as secondary therapy in patients with metastatic ovarian tumors refractory to standard chemotherapy who have not previously received Cisplatin Injection therapy.
- **Advanced Bladder Cancer:** Cisplatin Injection is indicated as a single agent for patients with transitional cell bladder cancer which is no longer amenable to local treatments, such as surgery and/or radiotherapy.

DOSAGE AND ADMINISTRATION

- **Metastatic Testicular Tumors:** The usual Cisplatin Injection dose for the treatment of testicular cancer in combination with other approved chemotherapeutic agents is 20 mg/m² IV daily for 5 days per cycle.
- **Metastatic Ovarian Tumors:** The usual 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 Injection is 600 mg/m² IV once every 4 weeks (DAY 1). In combination therapy, Cisplatin Injection and cyclophosphamide are administered sequentially. As a single agent, Cisplatin Injection should be administered at a dose of 100 mg/m² IV per cycle once every four weeks.
- **Advanced Bladder Cancer:** 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. For heavily pretreated patients an initial dose of 50 mg/m² per cycle repeated every 4 weeks is recommended.

A repeat course of Cisplatin Injection 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/mm³, WBC≥4000/mm³). Subsequent doses of Cisplatin Injection should not be given until an audiometric analysis indicates that auditory acuity is within normal limits.

CONTRAINDICATIONS

- History of hypersensitivity
- Preexisting renal impairment
- Myelosuppressed patients
- Hearing impairment

ADVERSE REACTIONS

- Nephrotoxicity
- Ototoxicity
- Hematologic: Leukopenia, thrombocytopenia, anaemia
- Gastrointestinal: Nausea, vomiting, diarrhea, anorexia
- Serum Electrolyte Disturbances
- Hyperuricemia
- Neurotoxicity
- Ocular Toxicity
- Anaphylactic-Like Reactions
- Hepatotoxicity

WARNING AND PRECAUTIONS

Cisplatin Injection should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available. Peripheral blood counts should be monitored weekly. Liver function should be monitored periodically. Neurologic examination should also be performed regularly.

Cisplatin produces cumulative nephrotoxicity which is potentiated by aminoglycoside antibiotics. The serum creatinine, blood urea nitrogen (BUN), creatinine clearance, and 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.

USE IN PREGNANCY AND LACTATION

Pregnancy Category D. 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. In mice cisplatin is teratogenic and embryotoxic. 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. Patients should be advised to avoid becoming pregnant. Cisplatin has been reported to be found in human milk, patients receiving cisplatin should not breast-feed.

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 altretamine (hexamethylmelamine) and cisplatin.

OVERDOSAGE

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. In addition, death can occur following overdosage.

PRECAUTION FOR HANDLING AND DISPOSAL

Caution should be exercised in handling the aqueous solution. Procedures for proper handling and disposal of anticancer drugs should be utilized. Several guidelines on this subject have been published. To minimize the risk of dermal exposure, always wear impervious gloves when handling vials and IV sets containing cisplatin. 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.

PREPARATION FOR INTRAVENOUS ADMINISTRATION

The aqueous solution should be used intravenously only and should be administered by IV infusion over a 6-to 8-hour period.

Pretreatment hydration with 1 to 2 liters of fluid infused for 8 to 12 hours prior to a Cisplatin Injection dose 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. Diluted Cisplatin injection solution should be used within 24 hours. Any unused portion should be discarded after that time in order to avoid risk of microbial contamination. Do not dilute Cisplatin Injection in just 5% Dextrose Injection. Adequate hydration and urinary output must be maintained during the following 24 hours.

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. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

PHARMACEUTICAL PRECAUTION

Cisplatin Injection is a sterile, multidose vial without preservatives. Store at or below 25 °C temperature. Do not refrigerate or freeze. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Cistor™ 10 IV Injection: Each box contains one multiple dose vial of Cisplatin BP 10 mg/10 mL injection.

Cistor™ 50 IV Injection: Each box contains one multiple dose vial of Cisplatin BP 50 mg/50 mL injection.

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
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TM TRADEMARK
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