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Cisplatin (Platinol, Platinol-AQ)

Drug type

- A platinum-containing, alkylating agent
- Often used in combination with other chemotherapy agents as well as monotherapy because of its relative lack of hematologic toxicity

Indications

- Invasive bladder malignancy
- Ovarian carcinoma
- Ovarian germ cell tumor carcinoma
- Testicular germ cell tumor

Unlabeled uses

- Adrenal cortex carcinoma
- Conditioning prior to allogeneic hematopoietic stem cell transplantation
- Endometrial carcinoma
- Gastric cancer
- Malignant tumor of cervix
- Malignant tumor of head and neck
- Metastatic breast carcinoma
- Metastatic malignant tumor of anus
- Multiple myeloma
- Neuroblastoma
- Neuroendocrine prostate carcinoma
- Osteosarcoma of bone
- Pancreatic carcinoma
- Progressive diffuse large B-cell lymphoma
- Small cell lung carcinoma and non-small cell lung cancer (NSCLC)

Mechanism of action

- Cell cycle nonspecific
- Complete mechanism of action is not entirely understood
- Appears to inhibit DNA synthesis by binding to DNA and disrupting its function
- Also enhances tumor immunogenicity

Dosage and administration

- Inadvertent substitution of cisplatin for carboplatin can result in potentially fatal overdose.
- Any dose >100 mg/m² should be verified
- Cisplatin is administered by IV infusion
 - Also intra-arterial injection and intraperitoneal injection
- Dose
 - Minimum: 25.95 mg/1.73 m²
 - Maximum: 173.0 mg/1.73 m²
- For optimum therapeutic results with minimum adverse effects, base dosage on clinical, renal, hematologic, and otic response and patient tolerance
- Consult published protocols for dosage, method, and sequence of administration
- At the usual dosage, do not give courses of therapy more frequently than once every 3–4 weeks
- Patients should be adequately hydrated before and for 24 hours after administration to ensure good urinary output and minimize nephrotoxicity.
- Needles, syringes, catheters, or IV administration sets containing aluminum parts that may come in contact with cisplatin should not be used for preparation or administration.

Pregnancy and lactation

- Pregnancy category D
 - Cisplatin may cause fetal harm when administered to a pregnant woman.
- Lactation
 - Absolute contraindication

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Cautions and adverse effects

- Cautions
 - Pediatric: Relative contraindication: risk of severe ototoxicity in children.
 - Geriatric: Increased risk of kidney, neurologic, hematologic toxicities; may need to reduce dose
- Adverse effects
 - Most frequent: Peripheral neuropathy (dose and duration dependent); bone marrow depression: anemia, leucopenia; hemolytic anemia, thrombocytopenic disorder; hyperuricemia; hypomagnesemia; nephrotoxicity; severe nausea and vomiting (antiemetic therapy is recommended); uric acid nephropathy gout
 - Less frequent: Allergic reactions (anaphylaxis, rash, urticaria); alopecia; anorexia; bronchospastic pulmonary disease; CNS toxicity, paresthesia; general weakness, and malaise; injection site sequelae
 - Rare:
 - Cardiovascular: cerebrovascular accident, hypotension, MI, tachyarrhythmia
 - GI: cramps and diarrhea
 - Electrolyte imbalances: hypocalcemia, hypokalemia, hyponatremia, hypophosphatemia
 - Neurotoxicity/CNS toxicity: Ototoxicity, seizure disorder, SIADH syndrome, and dysgeusia
 - Others: dehydration, facial edema, hiccups, optic neuritis, papilledema, sudden visual loss, thrombotic thrombocytopenic purpura

Drug interactions

- Nephrotoxic drugs
 - Concomitant use of amphotericin B and other potentially nephrotoxic drugs should probably be avoided during cisplatin administration
 - Cisplatin produces cumulative nephrotoxicity potentiated by aminoglycoside antibiotics
 - Risk may be lowered by giving aminoglycoside >2 weeks after cisplatin, if clinically feasible
- Ototoxic drugs
 - Monitor patients treated with cisplatin and other potentially ototoxic drugs (aminoglycoside antibiotics or loop diuretics) for signs of ototoxicity
- Antineoplastic agents
 - The antineoplastic activity of cisplatin and etoposide may be synergistic against some tumors
 - Elimination of etoposide may be impaired in patients previously treated with cisplatin
- Renally excreted drugs

- Cisplatin may alter renal elimination of bleomycin and methotrexate, possibly due to cisplatin-induced nephrotoxicity
- Consider possibility that cisplatin may affect elimination of renally excreted drugs
- Phenytoin
 - Serum concentrations of phenytoin may be decreased, possibly due to decreased absorption and/or increased metabolism of phenytoin
 - Monitor serum concentrations of phenytoin and make dosage adjustments when needed

What to tell your patient

- You have been prescribed cisplatin, an anti-cancer (also called *antineoplastic* or *cytotoxic*) chemotherapy drug, which is classified as an alkylating agent
- Although the exact mode of action is not known, cisplatin may stop cancer growth by binding to its DNA.
- Cisplatin is given as an infusion, usually through a vein. It also has been used as an infusion into the abdominal cavity. It is not available in pill form.
- Cisplatin is an irritant, a chemical that can cause inflammation of the vein through which it is given. It can also damage tissue if it escapes from the vein.
- Tell your nurse or doctor immediately if you experience pain or notice redness or swelling at the IV site while you are receiving cisplatin.
- Before and/or after the cisplatin infusion you will get extra IV fluids to protect your kidney function.
- The amount of cisplatin that you receive depends on many factors, including your height and weight, your general health or other health problems, and the type of cancer that you have. Your doctor will determine your dose and schedule.
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit is greater than the risk of side effects. Most people do not experience all of the side effects listed.
- Side effects are often predictable in terms of their onset and duration. They are almost always reversible and go away after treatment. There are many ways to help minimize or prevent side effects.
- Common side effects
 - Nausea and vomiting: May last up to one week after treatment; anti-nausea medication is given before the infusion, and a prescription is also given for use after
 - Kidney function: Effects are dose related; seen 10–20 days after treatment; are generally reversible

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- Blood test abnormalities: Low magnesium; low calcium; low potassium; low white blood cells (WBCs), may put you at increased risk for infection; low red blood cells (RBCs), called *anemia*
 - Less common side effects
 - Peripheral neuropathy, or decreased sensation and numbness and tingling of the extremities
 - High frequency hearing loss, or ringing in the ears
 - Loss of appetite
 - Taste changes, metallic taste
 - Temporary increases in blood tests measuring liver function
 - Hair loss
 - Your fertility, meaning your ability to conceive or father a child, may be affected by cisplatin after treatment. Please discuss this issue with your nurse.
 - Contact your health care provider immediately, day or night, if you should experience fever of 100.5°F (38°C) or higher, or chills (possible signs of infection), or any of the following:
 - Nausea (interferes with ability to eat and unrelieved with prescribed medication)
 - Vomiting (vomiting more than 4-5 times in a 24-hour period)
 - Diarrhea (4-6 episodes in a 24-hour period)
 - Extreme fatigue (unable to perform self-care)
 - Mouth sores/skin rash (painful redness, swelling or ulcers)
 - Eye irritation
 - Inability to eat or drink for 24 hours or have signs of dehydration: tiredness, thirst, dry mouth, dark and decrease amount of urine, or dizziness
 - Before starting this treatment, make sure you tell your doctor about any other medications you are taking (including prescription, over-the-counter, vitamins, herbal remedies, etc.).
 - Do not take aspirin or products containing aspirin unless your doctor specifically permits this.
 - Treatment with cisplatin may not be advisable if you have a history of severe allergic reaction to cisplatin, carboplatin, other platinum-containing formulations, or mannitol.
 - Do not receive any kind of immunization or vaccination without your doctor's approval while on this medication.
 - Inform your nurse or doctor if you are pregnant or may be pregnant prior to starting treatment. It is classified as Pregnancy Category D, which means cisplatin may be hazardous to the fetus.
 - For both men and women: Do not conceive a child (get pregnant) while on this medication. Barrier methods of contraception, such as condoms, are recommended. Discuss with your doctor when you may safely become pregnant or conceive a child after therapy.
 - Do not breast-feed while taking this medication. ■
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- Prepared by **Bette Weinstein Kaplan**. Reviewed by **Maribel Pereiras, PharmD, BCPS, BCOP**.
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