**DRUG NAME:** Cisplatin

**SYNONYM:** CDDP, cis-Diaminedichloroplatinum, cis-dichlorodiammineplatinum(II), cis-Patinum II, DDP

**COMMON TRADE NAME:** PLATINOL®, PLATINOL-AQ®, generic available

**CLASSIFICATION:** Platinum compound

*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.*

**MECHANISM OF ACTION:**
Cisplatin is similar to the bifunctional alkylating agents. It covalently binds to DNA and disrupts DNA function. After cisplatin enters the cells, the chloride ligands are replaced by water molecules. This reaction results in the formation of positively charged platinum complexes that react with the nucleophilic sites on DNA. These platinum complexes covalently bind to DNA bases using intra-strand and inter-strand cross-links creating cisplatin-DNA adducts thus preventing DNA, RNA and protein synthesis. This action is cell cycle phase-nonspecific. Cisplatin also has immunosuppressive, radiosensitizing, and antimicrobial properties.

**PHARMACOKINETICS:**

<table>
<thead>
<tr>
<th>Interpatient variability</th>
<th>systemic clearance resulting in variable blood platinum concentrations or AUCs¹⁰</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Absorption</td>
<td>not absorbed¹¹</td>
</tr>
<tr>
<td>Distribution</td>
<td>rapidly diffuses into tissues¹² highest concentrations found in the liver, prostate and kidney; rapidly distributed into pleural effusions and ascitic fluid</td>
</tr>
<tr>
<td></td>
<td>cross blood brain barrier? not readily⁹</td>
</tr>
<tr>
<td></td>
<td>volume of distribution¹³ ultrafilterable platinum*: 41 L/m²</td>
</tr>
<tr>
<td></td>
<td>plasma protein binding &gt;90%⁵,¹⁰,¹²</td>
</tr>
<tr>
<td>Metabolism</td>
<td>undergoes non-enzymatic conversion to several inactive metabolites which are highly bound to plasma proteins¹¹</td>
</tr>
<tr>
<td></td>
<td>active metabolite yes</td>
</tr>
<tr>
<td></td>
<td>inactive metabolite yes</td>
</tr>
<tr>
<td>Excretion</td>
<td>primarily in the urine⁷ urinary excretion of ultrafilterable platinum* was substantially greater after a 6-hour infusion than after a 15-minute injection¹⁴</td>
</tr>
<tr>
<td></td>
<td>urine &gt; 90%⁷; 25% excreted during the first 24 h⁶</td>
</tr>
<tr>
<td></td>
<td>feces insignificant</td>
</tr>
<tr>
<td></td>
<td>terminal half life of ultrafilterable platinum*: 20-45 min</td>
</tr>
<tr>
<td></td>
<td>terminal half life of total platinum*: 5 days or longer</td>
</tr>
<tr>
<td></td>
<td>clearance 6.3 mL/min/kg</td>
</tr>
<tr>
<td>Gender</td>
<td>no clinically important differences found</td>
</tr>
<tr>
<td>Elderly</td>
<td>no clinically important differences found</td>
</tr>
<tr>
<td>Children</td>
<td>terminal half life of ultrafilterable platinum* &lt; 1 h¹¹</td>
</tr>
<tr>
<td></td>
<td>terminal half life of total platinum* 24-72 h¹¹</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>no clinically important differences found</td>
</tr>
</tbody>
</table>

Adapted from standard reference unless specified otherwise.

*Ultrafilterable platinum consists of non-protein-bound intact drug and metabolites, total platinum consists of all platinum species, both protein-bound or –unbound. Note that it is the platinum that is usually measured.
USES:

**Primary uses:**
* Bladder cancer
Brain cancer
Cervical cancer
Esophageal cancer
Gastraic cancer
Germ cell tumours
Gestational trophoblastic neoplasia
Head and neck cancer
Lung cancer, non-small cell
Lung cancer, small cell
Lymphoma, Hodgkin’s disease
Lymphoma, non-Hodgkin’s
Mesothelioma
Nasopharyngeal cancer
Osteosarcoma
* Ovarian cancer
Prostate cancer
*Testicular cancer

**Other uses:**
Adrenal carcinoma
Anal cancer
Breast cancer
Choriocarcinoma
Endometrial cancer
Kidney cancer
Liver cancer
Lymphomas
Melanoma
Penile cancer
Sarcoma
Thyroid cancer

*Health Canada approved indication

SPECIAL PRECAUTIONS:

**Administer with caution** to individuals with pre-existing renal impairment, myelosuppression or hearing impairment.

**Breastfeeding** is not recommended as cisplatin is excreted in human milk.

**Carcinogenicity:** found to have a carcinogenic effect in laboratory animals.

**Contraindicated:** in patients who have a history of a hypersensitivity reaction to cisplatin or other platinum-containing compounds.

**Fertility:** Cisplatin therapy is associated with at least temporary infertility in the majority of patients. Among males receiving cisplatin for testicular cancer, almost all became azospermic within the first two cycles of therapy, but recovery of normal sperm morphology, motility, and sperm count occurred in 40% within 1.5-2 years.

**Hydration** is required to minimize nephrotoxicity. The manufacturer recommends pre-treatment hydration with 1 or 2 L of fluid infused 8-12 hours prior to a cisplatin dose. Hydration with NS, hypertonic saline infusion, and mannitol, or furosemide-induced diuresis is used to effectively decrease cisplatin-induced nephrotoxicity. Lower doses of cisplatin are given with less intensive hydration. For example, patients receiving doses of 35 mg/m² have been pre-treated with 500 mL NS over 1 hour, with no post-hydration. Patients receiving doses of 25 mg/m² have been pre-treated with vigorous oral hydration (e.g., 600-900 mL) the morning of treatment and 8 glasses (e.g., 2000 mL/day) daily for a few days following treatment. Please refer to the “Nephrotoxicity” paragraph, found below the Side Effects table for a suggested hydration guideline.

**Inadvertent substitution** of cisplatin for carboplatin can result in a potentially fatal overdosage. Precautions should be taken to avoid overdosing such as writing the cisplatin dose as a daily dose, not as a total cisplatin dose used in one course of therapy. The manufacturer recommends that an alerting mechanism be instituted to verify any order for cisplatin >100 mg/m² per course every 3-4 weeks.

**Mutagenicity:** shown to be a mild to moderate mutagen in the Ames test.
**Pregnancy:** FDA Pregnancy Category D. There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

**SIDE EFFECTS:**

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.  

<table>
<thead>
<tr>
<th>ORGAN SITE</th>
<th>SIDE EFFECT</th>
<th>ONSET</th>
</tr>
</thead>
<tbody>
<tr>
<td>allergy/immunology</td>
<td>hypersensitivity (rare)</td>
<td>I</td>
</tr>
<tr>
<td>auditory/hearing</td>
<td>ototoxicity (31%)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>audiogram abnormalities (24%)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>tinnitus (9%)</td>
<td>E</td>
</tr>
<tr>
<td>blood/bone marrow/febrile neutropenia</td>
<td>myelosuppression (25-30%) WBC nadir 18-23 days (range 7.5-45), platelet nadir 18-23 days (range 7.5-45), recovery 39 days (range 13-62)</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>anemia (25-30)%</td>
<td>I</td>
</tr>
<tr>
<td>cardiovascular (arrhythmia)</td>
<td>arrhythmias</td>
<td>E</td>
</tr>
<tr>
<td>cardiovascular (general)</td>
<td>bradycardia (rare)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>vascular toxicities may include myocardial infarction, cerebrovascular accident, thrombotic microangiopathy or cerebral arteritis</td>
<td>E</td>
</tr>
<tr>
<td>constitutional symptoms</td>
<td>hiccoughs</td>
<td>I</td>
</tr>
<tr>
<td>dermatology/skin</td>
<td>extravasation hazard: irritant</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>alopecia (uncommon)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>rash (uncommon)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>local soft tissue toxicity (rare)</td>
<td>E</td>
</tr>
<tr>
<td>endocrine</td>
<td>glucose intolerance</td>
<td>E</td>
</tr>
<tr>
<td>gastrointestinal</td>
<td>emetogenic potential: high</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>nausea and vomiting (&gt; 90%)</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>delayed nausea and vomiting</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>diarrhea</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>loss of taste</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>pancreatitis</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>stomatitis</td>
<td>E</td>
</tr>
<tr>
<td>ORGAN SITE</td>
<td>SIDE EFFECT</td>
<td>ONSET</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>hepatic</td>
<td>transient elevation of hepatic enzymes and bilirubin</td>
<td>I</td>
</tr>
<tr>
<td>metabolic/laboratory</td>
<td>elevated serum amylase</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td><strong>electrolyte disturbances</strong></td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>hyperuricemia</td>
<td></td>
</tr>
<tr>
<td>musculoskeletal</td>
<td>muscle cramps</td>
<td>E</td>
</tr>
<tr>
<td>neurology</td>
<td>autonomic neuropathy</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>dorsal column myelopathy</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>Lhermitte’s sign</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td><strong>neurotoxicity, usually peripheral neuropathies</strong></td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>seizures (rare)</td>
<td>E</td>
</tr>
<tr>
<td>ocular/visual</td>
<td>visual impairment (rare)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>altered colour perception</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>blurred vision</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>cerebral blindness (infrequent)</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>optic neuritis</td>
<td>E</td>
</tr>
<tr>
<td></td>
<td>papilledema</td>
<td>E</td>
</tr>
<tr>
<td>renal/genitourinary</td>
<td><strong>nephrotoxicity (28-36%)</strong></td>
<td>E</td>
</tr>
<tr>
<td>secondary malignancy</td>
<td>acute leukemia (rare)</td>
<td>L</td>
</tr>
<tr>
<td>syndromes</td>
<td>inappropriate antidiuretic hormone syndrome</td>
<td>E</td>
</tr>
</tbody>
</table>

Adapted from standard references\(^2\,15,16\) unless specified otherwise.

**Anemia** observed with cisplatin use may be caused by a decrease in erythropoietin or erythroid stem cells.\(^2\) Cisplatin has been shown to sensitize red blood cells, sometimes resulting in a direct Coombs’ positive hemolytic anemia.\(^6\)

**Electrolyte disturbances** can be serious and mainly includes hypomagnesemia, hypocalcemia and hypokalemia. Hypophosphatemia and hyponatremia have occurred in some patients receiving cisplatin combination regimens.\(^2\) These effects are due to renal tubular damage. Cisplatin greatly increases the urinary excretion of magnesium and calcium; increased excretion of potassium, zinc, copper and amino acids also occurs. Hypomagnesemia and or hypocalcemia may become symptomatic, with muscle irritability or cramps, clonus, tremor, carpopedal spasm and/or tetany. Children may be at greater risk for developing hypomagnesemia.

**Emetogenic effects** are common with cisplatin therapy and may be serotonin-mediated.\(^10\) **Acute** nausea and vomiting may occur within 1-6 (usually 2-3) hours after administration of cisplatin.\(^5\) This early period is the most severe and usually lasts 8 hours, but can last up to 24 hours. Various levels of nausea, vomiting and anorexia may persist for up to 5-10 days. **Delayed** nausea and vomiting can occur 24 hours or longer following chemotherapy when complete emetic control had been attained on the day of cisplatin therapy. The incidence and severity of cisplatin-induced nausea and vomiting appear to be increased in: females, the young, high doses, rapid infusion and combinations with other emetogenic drugs. Incidence and severity may be decreased in patients with a history of chronic alcohol use. **Acute** nausea and vomiting can be prevented by pre-treatment with a 5-HT\(_3\) antagonist (e.g., granisetron, ondansetron) plus a corticosteroid; this can be continued for the first 24 hours following chemotherapy. **Delayed** nausea and vomiting should not routinely be treated with 5-HT\(_3\) antagonists; although there is anecdotal evidence that some patients can benefit from 5-HT\(_3\) antagonists\(^{16}\), generally these agents are ineffective more than...
24 hours after chemotherapy. Corticosteroids are the cornerstone of the treatment for delayed nausea, although other combinations are widely used. Please refer to the BC Cancer Agency SCNAUSEA Protocol for more in-depth information.

**Nephrotoxicity** is a major concern when prescribing cisplatin. Renal dysfunction due to cisplatin may manifest as renal insufficiency, hypokalemia and hypomagnesemia. The risk for these adverse effects is related to the dose and interval of cisplatin and may be minimized by adequate hydration. Geriatric patients may also be at increased risk.

- The manufacturer recommends pre-treatment hydration with 1 or 2 L of fluid infused 8-12 hours prior to a cisplatin dose. Others suggest hydration with NS, hypertonic saline infusion, and mannitol, or furosemide-induced diuresis to effectively decrease cisplatin-induced nephrotoxicity.

Refer to protocol by which patient is being treated. Numerous hydration regimens exist. Hydration regimens should take into account the following conditions for the patient: adequate renal function, clinically euvoletic prior to administration of cisplatin, no contraindication to saline loading (e.g., uncompensated cardiac conditions, anasarca), and ability to comply with recommended oral hydration protocol, or expectation that volume status can be maintained (e.g., with fluids via enteral feeding tube or IV). Below is one suggested hydration regimen for adults.

<table>
<thead>
<tr>
<th>Cisplatin (mg/m²)</th>
<th>Hydration</th>
<th>Electrolyte Additives*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 80</td>
<td>4000 mL* NS over 4 h</td>
<td>KCl 20 mEq, MgSO₄ 1 g, Mannitol 30 g</td>
<td>inpatient or medical daycare unit admission to monitor urine output</td>
</tr>
<tr>
<td>60-80</td>
<td>2000 mL* NS over 2 h</td>
<td>KCl 20 mEq, MgSO₄ 1 g, Mannitol 30 g</td>
<td></td>
</tr>
<tr>
<td>40-60</td>
<td>1000 mL* NS over 1 h</td>
<td>KCl 10 mEq, MgSO₄ 0.5 g</td>
<td>includes regimens with cisplatin administered over multiple days</td>
</tr>
<tr>
<td>&lt;40</td>
<td>500 mL* NS over 30 min</td>
<td>none</td>
<td>includes regimens with cisplatin administered over multiple days</td>
</tr>
</tbody>
</table>

*Volume may include hydration associated with the administration of other drugs (e.g., other chemotherapy agents, supportive IV medications). The volumes and durations are minimum administration standards to accommodate the wide variation in clinical practice in delivery of cisplatin. They should be individualized based on the clinical situation, which may affect the hydration regimen and addition of electrolytes.

In children, for moderate to high-dose cisplatin give pre-hydration at 125mL/m²/h for a minimum of 2 hours to increase urine output to >100 mL/m²/h (>3 mL/kg/h). The hydration fluid most commonly used is D5/2NS + 10mEq/L KCL. In post-hydration maintain urine output at 65-100 mL/m²/h with oral/IV fluids. D5/2NS + 20 mEq/L KCL + 20 mEq MgSO₄ + mannitol 20 g/L is commonly used for IV post-hydration.

**Nervous system effects** are usually peripheral neuropathies and sensory in nature (e.g., paresthesias of the upper and lower extremities). They can also include motor difficulties (especially gait); reduced or absent deep-tendon reflexes and leg weakness may also occur. Peripheral neuropathy is cumulative and usually reversible, although recovery is often slow. Geriatric patients may be at greater risk for these cisplatin-induced neuropathies. Muscle cramps have been reported, and usually occurred in patients with symptomatic peripheral neuropathy who received relatively high cumulative doses of cisplatin. Lhermitte’s sign (a sensation during neck flexion resembling electric shock) often is present with cisplatin-induced neuropathy. The occurrence of Lhermitte’s sign may coincide with the onset of peripheral neuropathies, and can last for 2-8 months. When signs of neuropathy occur, cisplatin should be discontinued.

**Otic effects** include tinnitus, with or without clinical hearing loss, and occasional deafness. Ototoxicity is cumulative and irreversible and results from damage to the inner ear. These effects may be more severe in children than in adults.
The manufacturer recommends that audiograms be performed prior to initiating therapy and prior to each subsequent dose of drug. Initially, there is loss of high frequency acuity (4000 to 8000 Hz). When acuity is affected in the range of speech, cisplatin should be discontinued under most circumstances and carboplatin substituted where appropriate. Ototoxicity appears to be dose related. Higher cumulative doses, higher individual doses and administration by IV bolus resulted in more severe ototoxicity, corresponding with higher plasma levels of ultrafilterable platinum. Ototoxicity may be enhanced in patients with prior or simultaneous cranial irradiation. Vestibular ototoxicity may increase with increasing cumulative dosage and may be more likely to occur in patients with pre-existing vestibular dysfunction.

**Sensitivity reactions** can include anaphylactoid reactions consisting of facial edema, flushing, wheezing or respiratory difficulties, tachycardia, and hypotension. These reactions can occur within a few minutes after IV administration of cisplatin; diaphoresis, nasal stuffiness, rhinorrhea, conjunctivitis, generalized erythema, apprehension, and sensation of chest constriction may also occur. Cisplatin-induced anaphylactoid reactions usually have occurred after multiple cycles of cisplatin (e.g., at least 5 doses), but also can occur after the first dose. There is a case report of a patient who experienced an anaphylaxis to cisplatin following nine previous uncomplicated cycles. Some reactions may also be due to the mannitol that is given with cisplatin to prevent nephrotoxicity. Occasionally, patients who experienced anaphylactoid reactions have been safely retreated with cisplatin following pre-treatment with corticosteroids and/or antihistamines; however, such prophylaxis is not uniformly effective in preventing recurrence.

### INTERACTIONS:

<table>
<thead>
<tr>
<th>AGENT</th>
<th>EFFECT</th>
<th>MECHANISM</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>etoposide</td>
<td>synergistic antineoplastic activity against testicular, small cell lung and, non-small cell lung cancers</td>
<td>possible impaired elimination of etoposide in patients previously treated with cisplatin</td>
<td>some protocols are designed to take advantage of this effect; monitor toxicity closely</td>
</tr>
<tr>
<td>nephrotoxic drugs such as aminoglycoside antibiotics and amphotericin</td>
<td>increased risk of nephrotoxicity</td>
<td>cumulative nephrotoxicity</td>
<td>use with extreme caution during or shortly after cisplatin</td>
</tr>
<tr>
<td>ototoxic drugs such as aminoglycoside antibiotics or loop diuretics (e.g., ethacrynic acid, furosemide)</td>
<td>increased risk of ototoxicity</td>
<td>cumulative ototoxicity</td>
<td>carefully monitor for signs of ototoxicity</td>
</tr>
<tr>
<td>phenytoin</td>
<td>decreased phenytoin serum levels</td>
<td>decreased absorption and/or increased metabolism of phenytoin</td>
<td>monitor serum levels of phenytoin</td>
</tr>
<tr>
<td>pyridoxine&lt;sup&gt;26&lt;/sup&gt;</td>
<td>decrease in cisplatin activity</td>
<td>further investigation required</td>
<td>avoid concomitant use of pyridoxine with cisplatin</td>
</tr>
<tr>
<td>renally excreted drugs</td>
<td>increase the serum levels of renally excreted drugs</td>
<td>reduced renal function caused by cisplatin</td>
<td>monitor toxicity</td>
</tr>
</tbody>
</table>

Adapted from standard references unless specified otherwise.

### SUPPLY AND STORAGE:

**Injection:** Cisplatin is available as sterile, unpreserved; single-dose vials (10 mg/10 mL, 50 mg/50 mL and 100 mg/100 mL) at a concentration of 1 mg/mL. Unopened vials are stored at room temperature. Do not refrigerate or freeze cisplatin solutions as a precipitate will form. Protect from light.

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.
SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

Do not use IV needles, syringes or sets that have aluminum components in the preparation or administration of cisplatin. An interaction between aluminum and platinum will occur resulting in the formation of a black precipitate, accompanied with a loss of potency.

Diluted solution for infusion: Dilute the prepared cisplatin injection in 2 L of D51/2S or 0.3%NS, containing 37.5 g of mannitol. The solution is not preserved and should be used within 24 hours. Any unused portion should be discarded. In children, the administration volume of cisplatin should be maintained at >125 mL/m²/hr, and contain mannitol 15 g/m² and MgSO₄ 20 mEq/L. Urine output should be maintained at > 90 mL/m²/hr during administration.

Compatibility: The following are compatible with cisplatin via Y-site injection: allopurinol, aztreonam, bleomycin, chlorpromazine, cimetidine, cladribine, cyclophosphamide, dexamethasone, diphenhydramine, doxorubicin, doxorubicin liposome, droperidol, famotidine, filgrastim, fludarabine, fluorouracil, furosemide, ganciclovir, gatifloxacin, gemcitabine, granisetron, heparin, hydromorphone, leucovorin, linezolid, lorazepam, melphalan, methotrexate, methylprednisolone, metoclopamidine, mitomycin, morphine, ondansetron, paclitaxel, prochlorperazine, promethazine, propofol, ranitidine, sargramostim, teniposide, topotecan, vinblastine, vincristine, vinorelbine.

The following are compatible with cisplatin in the same syringe in certain concentrations: bleomycin, cyclophosphamide, doxapram, doxorubicin, droperidol, fluorouracil, furosemide, heparin, leucovorin, methotrexate, metoclopramide, mitomycin, vincristine.

The following are compatible with cisplatin in the same infusion bag in certain concentrations and diluents: carboplatin, cyclophosphamide with etoposide, etoposide, etoposide with floxuridine, etoposide with mannitol and KCl, floxuridine, floxuridine with leucovorin, hydroxyzine, ifosfamide, and ifosfamide with etoposide, leucovorin, magnesium, mannitol, ondansetron and paclitaxel.

The following solutions are compatible with cisplatin at the stated concentrations: cisplatin 50 mg, 500 mg, 300 mg in D51/2NS 1L; cisplatin 50 mg, 300 mg, 500 mg in D5NS 1L; cisplatin 50 mg, 100 mg, 200 mg in D51/2NS with mannitol 1.875%; cisplatin 300 mg in D5W 1L; cisplatin 50 mg, 100 mg, 167 mg, 200 mg, 300 mg, 500 mg, 600 mg, 900 mg in NS 1L; cisplatin 50 mg, 100 mg, 200 mg in 1/2NS.

Incompatibility: The following are incompatible with cisplatin via Y-site injection: amifostine, amphotericin, cefepime, piperacillin-tazobactam and thiopeta.

The following are incompatible with cisplatin in the same infusion solution at the stated concentrations: cisplatin 200 mg with etoposide 400 mg, mannitol 1.875%, KCl 20 mEq in NS 1L; cisplatin 200 mg with fluorouracil 1 g in NS 1L; cisplatin 500 mg with fluorouracil 10 g in 1L NS; cisplatin 67 mg with mesna 3.33 g in NS 1L; cisplatin 67 mg with mesna 110 mg in NS 1L; cisplatin 200 mg with paclitaxel 1.2 g in NS 1L; cisplatin 200 mg with thiopeta 1 g in NS 1L.

The following solutions are incompatible with cisplatin at the stated concentrations: cisplatin 100 mg/L in D5W 5%; cisplatin 75 mg/L in D5W; cisplatin 50 mg/L in Sodium bicarbonate 5%; cisplatin 500 mg/L in Sodium bicarbonate 5%.

PARENTERAL ADMINISTRATION:

| Subcutaneous | no information found |
| Intramuscular | no information found |
| Direct intravenous | not to be administered by the direct IV route |

BCCA administration guideline noted in bold, italics
Intermittent infusion  
50-100 mL of compatible IV solution, over 15-30 minutes

Continuous infusion  
in 1-2 L of compatible IV solution, over 6-24 hours  
(administration over 24 hours may decrease nausea, vomiting and nephrotoxicity)

Intraperitoneal  
has been used

Intrathecal  
no information found

Intrapleural  
has been used

Intra-arterial  
has been used

Intravesical  
has been used

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count. Dosage may be reduced, delayed or discontinued in patients with bone marrow suppression due to cytotoxic/radiation therapy or with other toxicities.

**Adults:**

<table>
<thead>
<tr>
<th>Cycle Length</th>
<th>BCCA usual dose noted in <strong>bold</strong>, <strong>italics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td></td>
</tr>
</tbody>
</table>
| 1 week\(^{29,30}\): | **25-40 mg/m^2 IV on day 1**  
(total dose per cycle 25-40 mg/m\(^2\)) |
| 2 weeks\(^{31}\):  | **30 mg/m^2 IV for one dose on days 1-3**  
(total dose per cycle 90 mg/m\(^2\)) |
| 3 weeks\(^{32-37}\):  | **20-100 mg/m^2 IV on day 1**  
(total dose per cycle 20-100 mg/m\(^2\)) |
| 3 weeks\(^{38}\):  | **60 mg/m^2 IV once daily for 2 consecutive days starting on day 1**  
(total dose per cycle 120 mg/m\(^2\)) |
| 3 weeks\(^{39}\):  | **20 mg/m^2 IV for one dose on days 1 and 5**  
(total dose per cycle 40 mg/m\(^2\)) |
| 3 weeks\(^{36}\):  | **30 mg/m^2 IV for one dose on days 1 and 8**  
(total dose per cycle 60 mg/m\(^2\)) |
| 3 weeks\(^{40-45}\):  | **25 mg/m^2 IV for one dose on days 1-3**  
(total dose per cycle 75 mg/m\(^2\)) |
| 3 weeks\(^{46-49}\):  | **20 mg/m^2 IV for one dose on days 1-5**  
(total dose per cycle 100 mg/m\(^2\)) |
| 4 weeks\(^{50,51}\):  | **70-100 mg/m^2 IV on day 1**  
(total dose per cycle 70-100 mg/m\(^2\)) |
| 4 weeks\(^{52,53}\):  | **25-30 mg/m^2 IV once daily for 3 consecutive days starting on day 1**  
(total dose per cycle 75-90 mg/m\(^2\)) |
Cisplatin

**BCCA usual dose noted in bold, italics**

**Cycle Length:**
- **6 weeks**: 75 mg/m² IV for one dose on day 1 (total dose per cycle 75 mg/m²)

**Concurrent radiation:**
- **1 week**: 40 mg/m² IV for one dose on day 1 (total dose per cycle 40 mg/m²)
- **2 weeks**: 100 mg/m² IV for one dose on day 1 (total dose per cycle 100 mg/m²)
- **3 weeks**: 100 mg/m² IV for one dose on day 1 (total dose per cycle 100 mg/m²)
- **4 weeks**: 25 mg/m² IV for 3 consecutive days starting on day 1 (total dose per cycle 75 mg/m²)

**Dosage in myelosuppression:** modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"

**Dosage in renal failure:**
- **Suggested dose modifications:**
  - Creatinine clearance mL/min
  - > 60
  - 45 - 59 75% cisplatin or go to carboplatin option (if available)
  - < 45 hold cisplatin or delay with additional IV fluids or go to carboplatin option (if available)

  \[
  \text{Calculated creatinine clearance} = \frac{N \times (140 - \text{Age}) \times \text{weight}}{\text{Serum Creatinine in } \mu\text{mol/L}}
  \]

  * For males N = 1.23; for females N=1.04

**Dosage in hepatic failure:** no adjustment required

**Dosage in dialysis:** removable by dialysis, but only within 3 h of administration

**Children:**

**Intravenous:**
- **1 week**: 30 mg/m² IV one dose on day 1
- **3 weeks**: 90 mg/m² IV one dose on day 1
- **3-4 weeks**: 60 mg/m² IV one dose on day 1 and day 2

**REFERENCES:**