Cisplatin: Drug information

(For additional information see "Cisplatin: Patient drug information" and see "Cisplatin: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Experienced physician:

Cisplatin 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.

Renal toxicity:

Cumulative renal toxicity associated with cisplatin is severe. Other major dose-related toxicities are myelosuppression, nausea, and vomiting.

Ototoxicity:

Ototoxicity, which may be more pronounced in children, and is manifested by tinnitus or loss of high frequency hearing and, occasionally, deafness, is significant.

Hypersensitivity reactions:

Anaphylactic-like reactions have occurred. Facial edema, bronchoconstriction, tachycardia, and hypotension may occur within minutes of cisplatin administration. Epinephrine, corticosteroids, and antihistamines have been effectively employed to alleviate symptoms.

Medication safety:

Exercise caution to prevent inadvertent cisplatin overdose. Doses greater than 100 mg/m^2/cycle once every 3 to 4 weeks are rarely used. Care must be taken to avoid inadvertent cisplatin overdose due to confusion with carboplatin or prescribing practices that fail to differentiate daily doses from total dose per cycle.

Brand Names: Canada

Cisplatin Injection; Cisplatin Injection BP; Cisplatin Injection, Mylan STD

Pharmacologic Category

Antineoplastic Agent, Alkylating Agent; Antineoplastic Agent, Platinum Analog

Dosing: Adult **VERIFY ANY CISPLATIN DOSE EXCEEDING 100 mg/m^2 PER COURSE.**

Pretreatment hydration with 1 to 2 L of IV fluid is recommended. Cisplatin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Roila 2016).

Bladder cancer, advanced: IV: 50 to 70 mg/m^2 every 3 to 4 weeks; heavily pretreated patients: 50 mg/m^2 every 4 weeks

Ovarian cancer, metastatic: IV:

Single agent: 100 mg/m^2 every 4 weeks

Combination therapy: 75 to 100 mg/m^2 every 4 weeks or (off-label dosing) 75 mg/m^2 every 3 weeks (Ozols 2003)

Intraperitoneal (off-label route): 100 mg/m^2 on day 2 of a 21-day treatment cycle (in combination with IV and intraperitoneal paclitaxel) for 6 cycles (Armstrong 2006)

Testicular cancer, metastatic: IV: 20 mg/m^2/day for 5 days repeated every 3 weeks (in combination with bleomycin and etoposide) (Cushing 2004; Saxman 1998)

Testicular germ cell tumor, malignant (off-label dosing): IV: 25 mg/m^2 on days 2 to 5 every 3 weeks (in combination with paclitaxel and ifosfamide) for 4 cycles (Kondagunta 2005) **or** 20 mg/m^2 on days 1 to 5 every 3 weeks (in combination with bleomycin and etoposide) for 4 cycles (Nichols 1998) **or** 20 mg/m^2 on days 1 to 5 every 3 weeks (in combination with etoposide and ifosfamide) for 4 cycles (Nichols 1998)

Breast cancer, triple-negative (off-label use): IV: Neoadjuvant therapy (single agent): 75 mg/m^2 on day 1 every 3 weeks for 4 cycles (Silver 2010). Additional data may be necessary to further define the role of cisplatin in this setting.

Cervical cancer (off-label use): IV: 75 mg/m^2 on day 1 every 3 weeks (in combination with fluorouracil and radiation) for 3 cycles (Morris 1999) **or** 70 mg/m^2 on day 1 every 3 weeks for 4 cycles (in combination with fluorouracil; cycles 1 and 2 given concurrently with radiation) (Peters 2000) **or** 50 mg/m^2 on day 1 every 4 weeks (in combination with radiation and fluorouracil) for 2 cycles (Whitney 1999)

Endometrial carcinoma, recurrent, metastatic, or high-risk (off-label use): IV: 50 mg/m^2 on day 1 every 3 weeks (in combination with doxorubicin ± paclitaxel) for 7 cycles or until disease progression or unacceptable toxicity (Fleming 2004)

Esophageal and gastric cancers (off-label uses): IV:

CF regimen: 100 mg/m^2 over 30 minutes on days 1 and 29 (preoperative chemoradiation; in combination with fluorouracil) (Tepper 2008)

ECF, ECX regimens: 60 mg/m^2 on day 1 every 21 days for up to 8 cycles in combination with epirubicin (E) and either fluorouracil (F) or capecitabine (X) (Cunningham 2008) **or**

ECF regimen: 60 mg/m^2 on day 1 every 21 days for 3 preoperative and 3 postoperative cycles in combination with epirubicin and fluorouracil (Cunningham 2006)

TCF or DCF regimen: 75 mg/m^2 on day 1 every 3 weeks (in combination with docetaxel and fluorouracil) until disease progression or unacceptable toxicity (Ajani 2007; Van Cutsem 2006)

Head and neck cancer (off-label use): IV:

Locally-advanced disease: 100 mg/m^2 every 3 weeks for 3 doses (with concurrent radiation) (Bernier 2004; Cooper 2004) **or** 75 mg/m^2 every 3 weeks (in combination with docetaxel and fluorouracil) for 4 cycles or until disease progression or unacceptable toxicity (if no disease progression after 4 cycles, chemotherapy was followed by radiation) (Vermorken 2007) **or** 100 mg/m^2 every 3 weeks (in combination with docetaxel and fluorouracil) for 3 cycles or until disease progression or unacceptable toxicity (chemotherapy was followed by chemoradiation) (Posner 2007)

Metastatic disease: 100 mg/m^2 every 3 weeks (in combination with fluorouracil and cetuximab) until disease progression or unacceptable toxicity or a maximum of 6 cycles (Vermorken 2008)

Hodgkin lymphoma, relapsed/refractory (off-label use): IV:

DHAP regimen: 100 mg/m^2 continuous infusion over 24 hours on day 1 for 2 cycles; median duration between cycle 1 and 2 was 16 days (in combination with dexamethasone and cytarabine) (Josting 2002)

ESHAP regimen: 25 mg/m^2/day on days 1 to 4 (in combination with etoposide, methylprednisolone, and cytarabine) every 3 to 4 weeks for 3 or 6 cycles (Aparicio 1999)

Malignant pleural mesothelioma (off-label use): IV: 75 mg/m^2 on day 1 of each 21-day cycle (in combination with pemetrexed) (Vogelzang 2003) **or** 100 mg/m^2 on day 1 of a 28-day cycle (in combination with gemcitabine) (Nowak 2002) **or** 80 mg/m^2 on day 1 of a 21-day cycle (in combination with gemcitabine) (van Haarst 2002)

Multiple myeloma (off-label use): IV: VDT-PACE regimen: 10 mg/m^2/day administered as a continuous infusion on days 1 to 4 of each cycle; repeat every 4 to 6 weeks (in combination with bortezomib, dexamethasone, thalidomide, doxorubicin, cyclophosphamide, and etoposide) (Lee 2003; Pineda-Roman 2008)

Non-Hodgkin lymphoma, relapsed/refractory: IV:

DHAP regimen: 100 mg/m^2 continuous infusion over 24 hours on day 1 every 3 to 4 weeks for 6 to 10 cycles (in combination with dexamethasone and cytarabine) (Velasquez 1988)

ESHAP regimen: 25 mg/m^2/day continuous infusion over 24 hours on days 1 to 4 every 3 to 4 weeks for 6 to 8 cycles (in combination with etoposide, methylprednisolone, and cytarabine) (Velasquez 1994)

Non-small cell lung cancer (NSCLC; off-label use): IV: **Note:** There are multiple cisplatin-containing regimens for the treatment of NSCLC. Listed below are several commonly used regimens:

100 mg/m^2 on day 1 every 4 weeks (in combination with etoposide) for 3 to 4 cycles; (Arriagada 2004), or

100 mg/m^2 on day 1 every 4 weeks (in combination with vinorelbine) (Kelly 2001; Wozniak 1998), or

100 mg/m^2 on day 1 every 4 weeks (in combination with gemcitabine) (Comella 2000), or

80 mg/m^2 on day 1 every 3 weeks (in combination with gemcitabine) (Ohe 2007), or

75 mg/m^2 on day 1 every 3 weeks (in combination with pemetrexed) for up to 6 cycles or until disease progression or unacceptable toxicity (Scagliotti 2008)

Osteosarcoma (off-label use; combination chemotherapy): Adults < 30 years: IV: 60 mg/m^2/day for 2 days on weeks 2, 7, 25, and 28 (neoadjuvant) or weeks 5, 10, 25, and 28 (adjuvant) in combination with methotrexate, leucovorin, doxorubicin, cyclophosphamide, bleomycin, and dactinomycin (Goorin 2003)

Penile cancer, metastatic (off-label use): IV: 25 mg/m^2 over 2 hours on days 1, 2, and 3 every 3 to 4 weeks (in combination with paclitaxel and ifosfamide) for 4 cycles (Pagliaro 2010)

Small cell lung cancer (off-label use): IV:

Limited-stage disease: 60 mg/m^2 on day 1 every 3 weeks for 4 cycles (in combination with etoposide and concurrent radiation) (Turrisi 1999)

Extensive-stage disease: 80 mg/m^2 on day 1 every 3 weeks (in combination with etoposide) for 4 cycles (Lara 2009) or a maximum of 8 cycles (Ihde 1994) **or** 60 mg/m^2 on day 1 every 4 weeks for 4 cycles (in combination with irinotecan) (Lara 2009)

Dosing: Pediatric

(For additional information see "Cisplatin: Pediatric drug information")

VERIFY ANY CISPLATIN DOSE EXCEEDING 100 mg/m^2 PER COURSE. Pretreatment hydration is recommended. . Cisplatin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Dupuis 2011).

Germ cell tumors (off-label use; combination chemotherapy): IV: 20 mg/m^2/day on days 1 to 5 or 100 mg/m^2 on day 1 of a 21-day treatment cycle (Pinkerton 1986)

Hepatoblastoma (off-label use; combination chemotherapy): IV: 80 mg/m^2 continuous infusion over 24 hours on day 1 of a 21-day treatment cycle (Pritchard 2000)

Medulloblastoma (off-label use; combination chemotherapy): IV: 75 mg/m^2 on either day 0 or day 1 of each chemotherapy cycle (Packer 2006)

Neuroblastoma, high-risk (off-label use; combination chemotherapy): IV: 50 mg/m^2/day on days 0 to 3 of a 21-day cycle (cycles 3 and 5) (Naranjo 2011) **or** 50 mg/m^2/day on days 1 to 4 (cycles 3, 5, and 7) (Kushner 1994)

Osteosarcoma (off-label use; combination chemotherapy): IV: 60 mg/m^2/day for 2 days on weeks 2, 7, 25, and 28 (neoadjuvant) or weeks 5, 10, 25, and 28 (adjuvant) in combination with methotrexate, leucovorin, doxorubicin, cyclophosphamide, bleomycin, and dactinomycin (Goorin 2003)

Dosing: Geriatric

Refer to adult dosing. Select dose cautiously and monitor closely in the elderly; may be more susceptible to nephrotoxicity and peripheral neuropathy.

Dosing: Renal Impairment

Note: The manufacturer(s) recommend that repeat courses of cisplatin should not be given until serum creatinine is <1.5 mg/dL and/or BUN is <25 mg/dL and use is contraindicated in preexisting renal impairment. The following adjustments have been recommended.

Aronoff 2007:

CrCl 10 to 50 mL/minute: Administer 75% of dose

CrCl <10 mL/minute: Administer 50% of dose

Hemodialysis: Partially cleared by hemodialysis

Administer 50% of dose posthemodialysis

Continuous ambulatory peritoneal dialysis (CAPD): Administer 50% of dose

Continuous renal replacement therapy (CRRT): Administer 75% of dose

Janus 2010: Hemodialysis: Reduce initial dose by 50%; administer post hemodialysis or on nondialysis days.

Kintzel 1995:

CrCl 46 to 60 mL/minute: Administer 75% of dose

CrCl 31 to 45 mL/minute: Administer 50% of dose

CrCl <30 mL/minute: Consider use of alternative drug

Dosing: Hepatic Impairment There are no dosage adjustments provided in the manufacturer's labeling. However, cisplatin undergoes nonenzymatic metabolism and predominantly renal elimination; therefore, dosage adjustment is likely not necessary.

Dosing: Obesity *ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs 2012).

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous:

Generic: 50 mg/50 mL (50 mL); 100 mg/100 mL (100 mL); 200 mg/200 mL (200 mL)

Solution, Intravenous [preservative free]:

Generic: 50 mg/50 mL (50 mL); 100 mg/100 mL (100 mL); 200 mg/200 mL (200 mL)

Generic Equivalent Available (US) Yes

Administration Cisplatin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Dupuis 2011; Roila 2016). Pretreatment hydration with 1 to 2 L of fluid is recommended prior to cisplatin administration; adequate post hydration and urinary output (>100 mL/hour) should be maintained for 24 hours after administration.

IV: Infuse over 6 to 8 hours (according to the manufacturer's labeling); has also been infused (off-label rates) over 30 minutes to 3 hours, at a rate of 1 mg/minute, or as a continuous infusion; infusion rate varies by protocol (refer to specific protocol for infusion details). Do not administer as a rapid IV injection. Also refer to specific protocol for information regarding recommended concomitant hydration and diuretics.

Intraperitoneal (off-label route): Solution was prepared in warmed saline and infused as rapidly as possible through an implantable intraperitoneal catheter (Armstrong 2006).

Needles or IV administration sets that contain aluminum should not be used in the preparation or administration; aluminum may react with cisplatin resulting in precipitate formation and loss of potency.

Vesicant (at higher concentrations); ensure proper needle or catheter placement prior to and during infusion; avoid extravasation.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); initiate sodium thiosulfate antidote; elevate extremity.

Sodium thiosulfate 1/6 M solution: Inject 2 mL into existing IV line for each 100 mg of cisplatin extravasated; then consider also injecting 1 mL as 0.1 mL subcutaneous injections (clockwise) around the area of extravasation, may repeat subcutaneous injections several times over the next 3 to 4 hours (Ener 2004).

Dimethyl sulfoxide (DMSO) may also be considered an option: Apply to a region covering twice the affected area every 8 hours for 7 days; begin within 10 minutes of extravasation; do not cover with a dressing (Perez Fidalgo 2012).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use

Bladder cancer, advanced: Treatment (as a single agent) of advanced bladder cancer (transitional cell) in patients who are no longer candidates for local therapy including surgery and/or radiation therapy

Ovarian cancer, metastatic: Treatment of metastatic ovarian cancer (in combination with other chemotherapy agents) in patients who have previously received appropriate surgery and/or radiation therapy, or as a single agent for refractory tumors in patients who have not previously received cisplatin

Testicular cancer, metastatic: Treatment of metastatic testicular cancer (in combination with other chemotherapy agents) in patients who have previously received appropriate surgery and/or radiation therapy

Use: Off-Label

Breast cancer (triple-negative); Cervical cancer; Endometrial carcinoma, recurrent, metastatic, or high-risk; Germ cell tumors, malignant (pediatric); Esophageal cancer; Gastric cancer; Head and neck cancer (locally advanced disease); Head and neck cancer (metastatic disease); Hepatoblastoma (pediatric); Hodgkin lymphoma; Malignant pleural mesothelioma; Medulloblastoma (pediatric); Multiple myeloma; Neuroblastoma; Non-Hodgkin lymphoma, relapsed/refractory; Non-small cell lung cancer; Osteosarcoma; Penile cancer (metastatic); Small cell lung cancer (extensive-stage disease); Small cell lung cancer (limited-stage disease); Anal carcinoma (metastatic); Central nervous system tumors; Gestational trophoblastic disease (refractory); Hepatobiliary cancer; Melanoma (metastatic); Neuroendocrine tumors; Pancreatic cancer (advanced); Primary CNS lymphoma; Prostate cancer; Thymoma/thymic carcinoma; Unknown primary cancers

Medication Safety Issues

Sound-alike/look-alike issues:

CISplatin may be confused with CARBOplatin, oxaliplatin

Platinol may be confused with Patanol

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Geriatric Patients: High-Risk Medication:

Beers Criteria: Cisplatin is identified in the Beers Criteria as a potentially inappropriate medication to be used with caution in patients 65 years and older because of the potential to cause or exacerbate syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatremia; monitor sodium concentration closely when initiating or adjusting the dose in older adults (Beers Criteria [AGS 2015]).

Administration issues:

Cisplatin doses >100 mg/m^2 once every 3 to 4 weeks are rarely used and should be verified with the prescriber.

Adverse Reactions

>10%:

Central nervous system: Neurotoxicity (peripheral neuropathy is dose and duration dependent)

Gastrointestinal: Nausea and vomiting (76% to 100%)

Genitourinary: Nephrotoxicity (28% to 36%; acute renal failure and chronic renal insufficiency)

Hematologic & oncologic: Anemia (≤40%), leukopenia (25% to 30%; nadir: Day 18 to 23; recovery: By day 39; dose related), thrombocytopenia (25% to 30%; nadir: Day 18 to 23; recovery: By day 39; dose related)

Hepatic: Increased liver enzymes

Otic: Ototoxicity (children 40% to 60%; adults 10% to 31%; as tinnitus, high frequency hearing loss)

1% to 10%: Local: Local irritation

<1%, postmarketing, and/or case reports: Alopecia (mild), ageusia, anaphylaxis, aortic thrombosis (Fernandes 2011), autonomic neuropathy, bradycardia (Schlumbrecht 2015), bronchoconstriction, cardiac arrhythmia, cardiac failure, cerebral arteritis, cerebrovascular accident, dehydration, diarrhea, extravasation, heart block, hemolytic anemia (acute), hemolytic-uremic syndrome, hiccups, hypercholesterolemia, hyperuricemia, hypocalcemia, hypokalemia, hypomagnesemia, hyponatremia, hypophosphatemia, hypotension, increased serum amylase, ischemic heart disease, leukoencephalopathy, Lhermitte's sign, myocardial infarction, neutropenic enterocolitis (Furonaka 2005), optic neuritis, pancreatitis (Trivedi 2005), papilledema, peripheral ischemia (acute), phlebitis (Tokuda 2014), reversible posterior leukoencephalopathy syndrome, seizure, SIADH, skin rash, tachycardia, tetany, thrombotic thrombocytopenic purpura, vision color changes, vision loss

Contraindications History of allergic reactions to cisplatin, other platinum-containing compounds, or any component of the formulation; preexisting renal impairment; myelosuppressed patients; hearing impairment

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: **[US Boxed Warning]: Myelosuppression is a major dose-related toxicity.**

• Extravasation: Cisplatin is a vesicant at higher concentrations, and an irritant at lower concentrations; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation. Local infusion site reactions may occur; monitor infusion site during administration.

• Gastrointestinal events: **[US Boxed Warning]: Nausea and vomiting are dose-related toxicities.** Cisplatin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Dupuis 2011; Roila 2016). Nausea and vomiting are dose-related and may be immediate and/or delayed. Diarrhea may also occur.

• Hypersensitivity reactions: **[US Boxed Warning]: Anaphylactic-like reactions have been reported; may include facial edema, bronchoconstriction, tachycardia, and hypotension and may occur within minutes of administration. Symptoms may be managed with epinephrine, corticosteroids, and/or antihistamines.**

• Hyperuricemia: Hyperuricemia has been reported with cisplatin use, and is more pronounced with doses >50 mg/m^2; consider antihyperuricemic therapy to reduce uric acid levels.

• Neurotoxicity: Severe (and possibly irreversible) neuropathies (including stocking-glove paresthesias, areflexia, and loss of proprioception/vibratory sensation) may occur with higher than recommended doses or more frequent administration; may require therapy discontinuation. Seizures, loss of motor function, loss of taste, leukoencephalopathy, and posterior reversible leukoencephalopathy syndrome (PRES [formerly RPLS]) have also been described.

• Ototoxicity: **[US Boxed Warning]: Ototoxicity, which may be more pronounced in children, is**

manifested by tinnitus and/or loss of high frequency hearing and occasionally deafness; may be significant. Ototoxicity is cumulative and may be severe. Audiometric testing should be performed at baseline and prior to each dose. Certain genetic variations in the thiopurine S-methyltransferase (TPMT) gene may be associated with an increased risk of ototoxicity in children administered conventional cisplatin doses (Pussegoda 2013). Controversy may exist regarding the role of TPMT variants in cisplatin ototoxicity (Ratain 2013; Yang 2013); the association has not been consistent across populations and studies. Children without the TPMT gene variants may still be at risk for ototoxicity. Cumulative dose, prior or concurrent exposure to other ototoxic agents (eg, aminoglycosides, carboplatin), prior cranial radiation, younger age, and type of cancer may also increase the risk for ototoxicity in children (Knight 2005; Landier 2014). Pediatric patients should receive audiometric testing at baseline, prior to each dose, and for several years after discontinuing therapy. An international grading scale (SIOP Boston scale) has been developed to assess ototoxicity in children (Brock 2012).

• Renal toxicity: **[US Boxed Warning]: Cumulative renal toxicity associated with cisplatin is severe.** Monitor serum creatinine, blood urea nitrogen, creatinine clearance, and serum electrolytes (calcium, magnesium, potassium, and sodium) closely. According to the manufacturer's labeling, use is contraindicated in patients with preexisting renal impairment and renal function must return to normal prior to administering subsequent cycles; some literature recommends reduced doses with renal impairment. Nephrotoxicity may be potentiated by aminoglycosides.

• Secondary malignancies: Secondary malignancies have been reported with cisplatin in combination with other chemotherapy agents.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Elderly: Select dose cautiously and monitor closely in elderly patients; they may be more susceptible to nephrotoxicity and peripheral neuropathy.

Other warnings/precautions:

• Medication safety (usual maximum dose per cycle): **[US Boxed Warning]: Doses >100 mg/m^2/cycle (once every 3 to 4 weeks) are rare; verify with the prescriber. Exercise caution to avoid inadvertent overdose due to potential sound-alike/look-alike confusion between CISplatin and CARBOplatin or prescribing practices that fail to differentiate daily doses from the total dose per cycle.** At the approved dose, cisplatin should not be administered more frequently than once every 3 to 4 weeks.

• Experienced physician: **[US Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician. Adequate diagnostic and treatment facilities and appropriate management of potential complications should be readily available.**

• Hydration: Patients should receive adequate hydration, with or without diuretics, prior to and for 24 hours after administration; serum electrolytes, particularly magnesium and potassium, should be monitored and replaced as needed during and after therapy.

Metabolism/Transport Effects None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Alpha-Lipoic Acid: May diminish the therapeutic effect of CISplatin. *Risk C: Monitor therapy*

Aminoglycosides: CISplatin may enhance the nephrotoxic effect of Aminoglycosides. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosphenytoin-Phenytoin: Platinum Derivatives may decrease the serum concentration of Fosphenytoin-Phenytoin. *Risk C: Monitor therapy*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Loop Diuretics: May enhance the nephrotoxic effect of CISplatin. Loop Diuretics may enhance the

ototoxic effect of CISplatin. *Risk C: Monitor therapy*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Taxane Derivatives: Platinum Derivatives may enhance the myelosuppressive effect of Taxane Derivatives. Administer Taxane derivative before Platinum derivative when given as sequential infusions to limit toxicity. *Risk D: Consider therapy modification*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Topotecan: Platinum Derivatives may enhance the adverse/toxic effect of Topotecan. *Risk D: Consider therapy modification*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live).

Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Vinorelbine: CISplatin may enhance the adverse/toxic effect of Vinorelbine. Specifically, the combination may be associated with a higher risk of granulocytopenia. *Risk C: Monitor therapy*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

Adverse effects have been observed in animal reproduction studies. Women of childbearing potential should be advised to avoid pregnancy during treatment. May case fetal harm if administered during pregnancy.

Breast-Feeding Considerations

Cisplatin is excreted in breast milk. Breast-feeding is not recommended by the manufacturer.

Dietary Considerations

Some products may contain sodium.

Monitoring Parameters

Renal function (serum creatinine, BUN, CrCl [baseline and before each cycle]); electrolytes (particularly calcium, magnesium, potassium, and sodium [baseline and before each cycle]); CBC with differential and platelet count (weekly); liver function tests (periodic); urine output, urinalysis; audiography (baseline and prior to each subsequent dose, and following treatment in children), neurologic exam (with high dose); monitor infusion site during infusion

Mechanism of Action

Inhibits DNA synthesis by the formation of DNA cross-links; denatures the double helix; covalently binds to DNA bases and disrupts DNA function; may also bind to proteins; the *cis*-isomer is 14 times more cytotoxic than the *trans*-isomer; both forms cross-link DNA but cis-platinum is less easily recognized by cell enzymes and, therefore, not repaired. Cisplatin can also bind two adjacent guanines on the same strand of DNA producing intrastrand cross-linking and breakage.

Pharmacodynamics/Kinetics

Distribution: IV: Rapidly into tissue; high concentrations in kidneys, liver, ovaries, uterus, and lungs

Protein binding: >90% (O'Dwyer 2000)

Metabolism: Nonenzymatic; inactivated (in both cell and bloodstream) by sulfhydryl groups; covalently binds to glutathione and thiosulfate

Half-life elimination:

Children: Free drug: 1.3 hours; Total platinum: 44 hours

Adults: Initial: 14 to 49 minutes; Beta: 0.7 to 4.6 hours; Gamma: 24 to 127 hours (O'Dwyer 2000)

Excretion: Urine (>90%); feces (minimal)

Pricing: US

Solution (CISplatin Intravenous)

50 mg/50 mL (50 mL): $21.66

100 mg/100 mL (100 mL): $42.00

200 mg/200 mL (200 mL): $86.64

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Abiplatin (IL, NZ, TW); Accocit (CR, DO, GT, HN, NI, PA, SV); Bioplatino (PE); Blastolem (CL, CO, CR, DO, GT, HN, NI, PA, SV); Blastolem RU (MX); Cesalin (BD, LK); Ciscan (ID); Cisly (LU); Cispatin (KR); Cisplan (KR); Cisplat (IN); Cisplatin (AU, ID, IN, NZ); Cisplatin Ebewe (HU); Cisplatin medac (LU); Cisplatin Teva (HU); Cisplatin-Ebewe (MY); Cisplatine-Lilly (LU); Cisplatino (CO, EC, PE); Cisplatinum Cytosafe-Delta West (LU); Cisplatyl (FR, KW, QA, SA); Cisteen (PH); Citoplatino (IT); Citoplax (BR); Cysplack (PH); Cytoplatin (LB); Elvecis (AR); Fangtan (CN); Incel (BR, PY); Kemocarb (VN); Kemoplat (IN, PH, SG, TW, UA); Lederplatin (DK); Noveldexis (CR, DO, GT, HN, MX, NI, PA, SV); Oncotin (PH); P&U Cisplatin (ZA); Placis (ES, JO, TH, TR); Platamine (AE, BH, CY, HR, IQ, IR, IT, JO, KW, LB, LY, OM, QA, SA, SY, YE); Platiblastin (CH, DE); Platicin (LK); Platidiam (BG, CZ, HN, HU, PL, RU); Platimit (HR); Platin (PH); Platinex (BD, HR, IT, LK); Platinol (AR, AT, BE, CH, EE, EG, FI, GR, LU, SE, UY); Platistil (PT); Platistin (FI, SE); Platistine (LU); Platol (ET); Platosin (GB, KR, MY, NL, PK, RO, TH); Platysan (UA); Randa (JP); Sicatem (PY); Sinplatin (BG, RO); Tecnoplatin (MX)

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