CISPLATIN:

Class: Antineoplastic Agent, Alkylating Agent , Platinum Analog
Indications: - Bladder cancer, advanced -Ovarian cancer, metastatic -Testicular cancer,

- metastaticCervical cancer -Endometrial carcinoma, recurrent, metastatic, or high-risk

-Head and neck cancer -Malignant pleural mesothelioma - NSCLC Ovarian cancerSCLC

-Testicular germ cell tumor, malignant

Available dosage form in the hospital: 10MG/ML || 50 MG / 50 ML || 50MG/100ML VIAL || 0.5MG /ML || 20ML || 50ml INJ

Trade Names: Abiplatin (IL, NZ, TW); Bioplatino (PE); Blastolem (CN, CO); Blastolem RU (MX); Cisly (LU); Cispatin

Dosage: **VERIFY ANY CISPLATIN DOSE EXCEEDING 100 mg/m^2 PER COURSE.**Pretreatment hydration with 1-2 L of I.V. fluid is recommended. Details concerning dosing in combination regimens should also be consulted.

-**Bladder cancer, advanced:** I.V.: 50-70 mg/m^2 every 3-4 weeks; heavily pretreated patients: 50 mg/m^2 every 4 weeks

-**Ovarian cancer, metastatic: I.V.:**

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

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

-**Testicular cancer, metastatic**: I.V.: 20 mg/m^2/day for 5 days repeated every 3 weeks (Cushing, 2004; Saxman, 1998)

-**Cervical cancer (unlabeled use):** I.V.: 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 (unlabeled use)**: I.V.: 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)

-**Head and neck cancer (unlabeled use): I.V.:**

-*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)

-**Malignant pleural mesothelioma (unlabeled use):** I.V.: 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)

-**NSCLC (unlabeled use):** I.V.: 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 3-4 cycles; (Arriagada, 2007), 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)

-**Ovarian cancer (unlabeled route):** Intraperitoneal: 75-100 mg/m^2 on day 2 of a 21-day treatment cycle (in combination with I.V. and intraperitoneal paclitaxel) for 6 cycles (Armstrong, 2006; NCCN Ovarian Cancer guidelines, v.1.2013)

-**SCLC (unlabeled use):** I.V.:

-*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)

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

Geriatric

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

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 pre-existing renal impairment. The following adjustments have been recommended.

-Aronoff, 2007:

- Cl_{cr} 10-50 mL/minute: Administer 75% of dose
- Cl_{cr} <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:

- Cl_{cr} 46-60 mL/minute: Administer 75% of dose
- Cl_{cr} 31-45 mL/minute: Administer 50% of dose
- Cl_{cr} <30 mL/minute: Consider use of alternative drug

Hepatic Impairment:

No dosage adjustment provided in 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).

Common side effect:

>10%:

Central nervous system: Neurotoxicity: Peripheral neuropathy is dose- and duration-dependent.

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

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

Hepatic: Liver enzymes increased

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

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

1% to 10%: Local: Tissue irritation

Pregnancy Risk Factor: D