CARBOPLATIN:

Class: Antineoplastic Agent, Alkylating agent,Platinum Analog

Indications: - Ovarian cancer, advanced - Bladder cancer - Breast cancer, metastatic
- Cervical cancer, recurrent or metastatic - Endometrial cancer
- Esophageal cancer - Head and neck cancer - Hodgkin's lymphoma, relapsed or refractory
- Malignant pleural mesothelioma - Melanoma, advanced or metastatic
- Non-Hodgkin's lymphomas, relapsed or refractory
- Nonsmall cell lung cancer - Sarcomas: Ewing's sarcoma, osteosarcoma
- Sarcomas: Ewing's sarcoma, osteosarcoma - Testicular cancer
- Thymic malignancies - Thymic malignancies

Available dosage form in the hospital: 150 MG VIAL|| 450MG VIAL || 10mg\ml 5ML VIAL

Trade Names: Actoplatin (ID); Bagotanilo (MX); Balidon (CO); Biovinate (PH); Biplatinex (VE); Blastocarb (CN); Blastocarb RU (MX); Bobei (CL); Carboplat (AR, DE, MX); Carboplatin (AU, DK, IL, NO, NZ)

Dosage: Details concerning dosing in combination regimens should also be consulted.**Note:** Doses for adults are commonly calculated by the target AUC using the Calvert formula, where**Total dose (mg) = Target AUC x (GFR + 25)**. If estimating glomerular filtration rate (GFR) instead of a measured GFR, the Food and Drug Administration (FDA) recommends that clinicians consider capping estimated GFR at a maximum of 125 mL/minute to avoid potential toxicity.

-**Ovarian cancer, advanced**: I.V.: 360 mg/m^2 every 4 weeks (as a single agent) or 300 mg/m^2 every 4 weeks (in combination with cyclophosphamide) or Target AUC 4-6 (single agent; in previously-treated patients)

Unlabeled dosing for advanced ovarian cancer: I.V.: Target AUC 5-7.5 every 3 weeks (in combination with paclitaxel) (Ozols, 2003; Parmar, 2003) or Target AUC 5 every 3 weeks (in combination with docetaxel) (Vasey, 2004)

-**Bladder cancer (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with gemcitabine and paclitaxel) (Hainsworth, 2005) or Target AUC 5 every 3 weeks (in combination with gemcitabine) (Bamias, 2006) or Target AUC 6 every 3 weeks (in combination with paclitaxel) (Vaughn, 2002)

-**Breast cancer, metastatic (unlabeled use):** I.V.: Target AUC 6 every 3 weeks (in combination with trastuzumab and paclitaxel) (Robert, 2006) or Target AUC 6 every 3 weeks (in combination with trastuzumab and docetaxel) (Pegram, 2004; Valero, 2011)

-**Cervical cancer, recurrent or metastatic (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with paclitaxel) (Pectasides, 2009) or Target AUC 5-6 every 4 weeks (in combination with paclitaxel) (Tinker, 2005) or 400 mg/m^2 every 28 days (as a single agent) (Weiss, 1990)

-**Endometrial cancer (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with paclitaxel) (Pectasides, 2008) or Target AUC 2 on days 1, 8, and 15 every 28 days (in combination with paclitaxel) (Secord, 2007)

-**Esophageal cancer (unlabeled use):** I.V.: Target AUC 2 on days 1, 8, 15, 22, and 29 for 1 cycle (in combination with paclitaxel) (van Meerten, 2006) or Target AUC 5 every 3 weeks (in combination with paclitaxel) (El-Rayes, 2004)

-**Head and neck cancer (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with cetuximab) (Chan, 2005) or Target AUC 5 every 3 weeks (in combination with cetuximab and fluorouracil) (Vermorken, 2008) or 300 mg/m^2 every 4 weeks (in combination with fluorouracil) (Forastiere, 1992) or Target AUC 6 every 3 weeks (in combination with paclitaxel) (Clark, 2001)

-**Hodgkin's lymphoma, relapsed or refractory (unlabeled use):** I.V.: Target AUC 5 (maximum dose 800 mg) for 2 cycles (in combination with ifosfamide and etoposide) (Moskowitz, 2001)

-**Malignant pleural mesothelioma (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with pemetrexed) (Castagneto, 2008; Ceresoli, 2006)

-**Melanoma, advanced or metastatic (unlabeled use):** I.V.: Target AUC 2 days on 1, 8, and 15 every 4 weeks (in combination with paclitaxel) (Rao, 2006)

-**Non-Hodgkin's lymphomas, relapsed or refractory (unlabeled use):** I.V.: Target AUC 5 (maximum dose 800 mg) per cycle for 3 cycles (in combination with rituximab, ifosfamide and etoposide) (Kewalramani, 2004)

-**Nonsmall cell lung cancer (unlabeled use):** I.V.: Target AUC 6 every 3-4 weeks (in combination with paclitaxel) (Ramalingam, 2008; Schiller, 2002; Strauss, 2008) orTarget AUC 6 every 3 weeks (in combination with bevacizumab and paclitaxel) (Sandler, 2006) or Target AUC 5 every 3 weeks (in combination with pemetrexed) (Gronberg, 2009) or in combination with radiation therapy and paclitaxel (Belani, 2005):

Target AUC 6 every 3 weeks for 2 cycles or

Target AUC 6 every 3 weeks for 2 cycles; then target AUC 2 weekly for 7 weeks or

Target AUC 2 every week for 7 weeks; then target AUC 6 every 3 weeks for 2 cycles

-**Sarcomas: Ewing's sarcoma, osteosarcoma (unlabeled uses):** I.V.: 400 mg/m^2/day for 2 days every 21 days (in combination with ifosfamide and etoposide) (van Winkle, 2005)

-**Small cell lung cancer (unlabeled use):** I.V.: Target AUC 6 every 3 weeks (in combination with etoposide) (Skarlos, 2001) or Target AUC 5 every 3 weeks (in combination with irinotecan) (Hermes, 2008) or Target AUC 5 every 28 days (in combination with irinotecan) (Schmittel, 2006)

-**Testicular cancer (unlabeled use):** I.V.: Target AUC 7 as a one-time dose (Oliver, 2011) or 700 mg/m^2/day for 3 days beginning 5 days prior to peripheral stem cell infusion (in combination with etoposide) for 2 cycles (Einhorn, 2007)

-**Thymic malignancies (unlabeled use):** I.V.: Target AUC 5 every 3 weeks (in combination with paclitaxel) (Lemma, 2008)

-**Unknown primary adenocarcinoma (unlabeled use):** I.V.: Target AUC 6 every 3 weeks (in combination with paclitaxel) (Briasoulis, 2000) or Target AUC 6 every 3 weeks (in combination with docetaxel) (Greco, 2000) or Target AUC 6 every 3 weeks (in combination with paclitaxel and etoposide) (Hainsworth, 2006) or Target AUC 5 every 3 weeks (in combination with paclitaxel and gemcitabine) (Greco, 2002).

Geriatric

The Calvert formula should be used to calculate dosing for elderly patients. Refer to adult dosing.

Renal impairment: **Note:** Dose determination with Calvert formula uses GFR and, therefore, inherently adjusts for renal dysfunction.

The manufacturer's labeling recommends the following dosage adjustment guidelines for single-agent therapy: Adults:

- Baseline Cl_{cr} 41-59 mL/minute: Initiate at 250 mg/m^2 and adjust subsequent doses based on bone marrow toxicity
- Baseline Cl_{cr} 16-40 mL/minute: Initiate at 200 mg/m^2 and adjust subsequent doses based on bone marrow toxicity

- Baseline $Cl_{cr} \leq 15$ mL/minute: No dosage adjustment provided in manufacturer's labeling

The following dosage adjustments have also been recommended:

Adults (**Note:** For dosing based on **mg/m^2**):
- GFR >50 mL/minute: No dosage adjustment necessary
- GFR 10-50 mL/minute: Administer 50% of the dose
- GFR <10 mL/minute: Administer 25% of the dose
- Hemodialysis: Administer 50% of dose
- Continuous ambulatory peritoneal dialysis (CAPD): Administer 25% of dose
- Continuous renal replacement therapy (CRRT): 200 mg/m^2

Janus, 2010: Hemodialysis: Carboplatin dose (mg) = Target AUC x 25; administer on a nondialysis day, hemodialysis should occur between 12-24 hours after carboplatin dose

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling; however, carboplatin undergoes minimal hepatic metabolism therefore dosage adjustment may not be needed.

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Dosing based on GFR should be considered in obese patients; GFR should not exceed 125 mL/minute (Griggs, 2012).

Dosing: Adjustment for Toxicity

Platelets <50,000 cells/mm^3 or ANC <500 cells/mm^3: Administer 75% of dose

Common side effect:

>10%:

Central nervous system: Pain (23%)

Endocrine & metabolic: Hyponatremia (29% to 47%), hypomagnesemia (29% to 43%), hypocalcemia(22% to 31%), hypokalemia (20% to 28%)

Gastrointestinal: Vomiting (65% to 81%), abdominal pain (17%), nausea (without vomiting: 10% to 15%)

Hematologic: Myelosuppression (dose related and dose limiting; nadir at ~21 days with single-agent therapy), anemia (71% to 90%; grades 3/4: 21%), leukopenia (85%; grades 3/4: 15% to 26%), neutropenia (67%; grades 3/4: 16% to 21%), thrombocytopenia (62%; grades 3/4: 25% to 35%)

Hepatic: Alkaline phosphatase increased (24% to 37%), AST increased (15% to 19%)

Neuromuscular & skeletal: Weakness (11%)

Renal: Creatinine clearance decreased (27%), BUN increased (14% to 22%)

Miscellaneous: Hypersensitivity/allergic reaction (2% to 16%)

1% to 10%:

Central nervous system: Neurotoxicity (5%)

Dermatologic: Alopecia (2% to 3%)

Gastrointestinal: Constipation (6%), diarrhea (6%), stomatitis/mucositis (1%), taste dysgeusia (1%)

Hematologic: Bleeding (5%), hemorrhagic complications (5%)

Hepatic: Bilirubin increased (5%)

Neuromuscular & skeletal: Peripheral neuropathy (4% to 6%)

Ocular: Visual disturbance (1%)
Otic: Ototoxicity (1%)
Renal: Creatinine increased (6% to 10%)
Miscellaneous: Infection (5%)

Pregnancy Risk Factor: D