Oxaliplatin:

Class:

- Alkylating Agent , Antineoplastic Agent, Platinum Analog

Indications:

- Treatment of stage III colon cancer (adjuvant) after complete resection of primary tumor;
- treatment of advanced colorectal cancer

Unlabeled use :

- Treatment of esophageal cancer,
- gastric cancer,
- hepatobiliary cancer (advanced),
- non-Hodgkin's lymphoma (refractory), o
- varian cancer (advanced, platinum-pretreated),
- pancreatic cancer (advanced),
- testicular cancer (refractory)

Available dosage form in the hospital:

50 mg vial

Trade Names:

Crisapla , Dacotin , Dacplat , **Eloxatin** , Entia , Henplatin , Liplatin , Olipcis , Oplat , Oxalem , Oxalip ,Oxaltic , Oxaltie , Oxapla , Oxerin , Oxitan , Oxitel , Oxol , OXP , Platinox , Pleoxtin , Rexta , Riptam , Sindoxplatin , Xaliplat , Zildox .

Dosage: **Note:** Oxaliplatin is associated with a moderate emetic potential; antiemetics are recommended to prevent nausea and vomiting. Details concerning dosing in combination regimens should also be consulted. I.V.:

-Advanced colorectal cancer: I.V.: 85 mg/m^2 every 2 weeks until disease progression or unacceptable toxicity (in combination with fluorouracil/leucovorin)

-Stage III colon cancer (adjuvant): I.V.: 85 mg/m^2 every 2 weeks for 6 months (12 cycles; in combination with fluorouracil/leucovorin)

-Colon/colorectal cancer (unlabeled doses or combinations): I.V.: 85 mg/m^2/dose on days 1, 15, and 29 of an 8-week treatment cycle in combination with fluorouracil/leucovorin (Kuebler, 2007) **or** 85 mg/m^2 every 2 weeks in combination with fluorouracil/leucovorin/irinotecan (Falcone, 2007) **or** 130 mg/m^2 every 3 weeks in combination with capecitabine (Cassidy, 2008; Haller, 2011)

-Esophageal/gastric cancers (unlabeled use; as part of a combination chemotherapy regimen): I.V.: 85 mg/m^2 every 2 weeks in combination with docetaxel, leucovorin, and fluorouracil (Al-Batran, 2008) **or** 85 mg/m^2 every 2 weeks in combination with leucovorin and fluorouracil (Conroy, 2010) **or** 130 mg/m^2 every 3 weeks in combination with epirubicin and either capecitabine or fluorouracil (Cunningham, 2008)

or

Gastric cancer:* I.V: 100 mg/m^2 every 2 weeks in combination with leucovorin and fluorouracil (Louvet, 2002) **or 130 mg/m^2 every 3 weeks in combination with capecitabine (Bang, 2012)

-Hepatobiliary cancer, advanced (unlabeled use; as part of a combination chemotherapy regimen): I.V.: 100 mg/m^2 every 2 weeks (Andre, 2004) **or**130 mg/m^2 every 3 weeks (Nehls, 2008)

-Non-Hodgkin's lymphoma, refractory (unlabeled use; as part of a combination chemotherapy regimen): I.V.: 25 mg/m^2/day for 4 days every 4 weeks (Tsimberidou, 2008) **or** 100 mg/m^2 every 3 weeks (Lopez, 2008; Rodriguez, 2007) **or** 130 mg/m^2 every 3 weeks (Chau, 2001)

-Ovarian cancer, advanced (unlabeled use): I.V.: 130 mg/m^2 every 3 weeks (Dieras, 2002; Piccart, 2000)

-Pancreatic cancer, advanced (unlabeled use; as part of a combination chemotherapy regimen): I.V.: 85 mg/m^2 every 2 weeks (Conroy, 2005; Conroy, 2011; Pelzer, 2011) **or** 100 mg/m^2 every 2 weeks (Louvet, 2005) **or** 110-130 mg/m^2 every 3 weeks (Xiong, 2008)

-Testicular cancer, refractory (unlabeled use; in combination with gemcitabine): I.V.: 130 mg/m^2 every 3 weeks in combination with gemcitabine (De Georgi, 2006; Kollmannsberger, 2004; Pectasides, 2004) **or** 130 mg/m^2 every 3 weeks in combination with gemcitabine and paclitaxel) (Bokemeyer, 2008).

Geriatric

No dosage adjustment necessary. Refer to adult dosing.

Renal Impairment:

Manufacturer's recommendations:

**U.S. labeling:*

-Cl_{cr} ≥30 mL/minute: No dosage adjustment necessary.

-Cl_{cr} <30 mL/minute: Reduce dose from 85 mg/m^2 to 65 mg/m^2.

**Canadian labeling:* Cl_{cr} <30 mL/minute: Use is contraindicated.

Alternate recommendations: Cl_{cr} ≥20 mL/minute: In a study with a limited number of patients with mild-to-moderate impairment, defined by the authors as Cl_{cr} 20-59 mL/minute (determined using 24-hour urine collection), oxaliplatin was well-tolerated, suggesting a dose reduction may not be necessary in patients with Cl_{cr} ≥20 mL/minute receiving every-3-week dosing (dose range: 80-130 mg/m^2 every 3 weeks) (Takimoto, 2003).

Hepatic Impairment:

Mild, moderate, or severe impairment: No dosage adjustment necessary (Doroshow, 2003; Synold, 2007).

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).

Dosing: Adjustment for Toxicity

-Acute toxicities: Longer infusion time (6 hours) may mitigate acute toxicities (eg, pharyngolaryngeal dysesthesia).

-Neurosensory events:

1.Persistent (>7 days) grade 2 neurosensory events:

- Adjuvant treatment of stage III colon cancer: Reduce dose to 75 mg/m^2
- Advanced colorectal cancer: Reduce dose to 65 mg/m^2

Consider withholding oxaliplatin for grade 2 neuropathy lasting >7 days despite dose reduction.

2.Persistent (>7 days) grade 3 neurosensory events:

**U.S. labeling:* Consider discontinuing oxaliplatin.

**Canadian labeling:*

- Adjuvant treatment of stage III colon cancer: Discontinue oxaliplatin.
- Advanced colorectal cancer: Reduce dose to 65 mg/m^2; if not resolved prior to next cycle, then discontinue.

-Gastrointestinal toxicity (grade 3/4):

- Adjuvant treatment of stage III colon cancer: Delay next dose until recovery from toxicity, then reduce dose to 75 mg/m^2.
- Advanced colorectal cancer: Delay next dose until recovery from toxicity, then reduce dose to 65 mg/m^2.

-Hematologic toxicity (grade 4 neutropenia or grade 3/4 thrombocytopenia):

- Adjuvant treatment of stage III colon cancer: Delay next dose until neutrophils recover to ≥1500/mm^3 and platelets recover to ≥75,000/mm^3, then reduce dose to 75 mg/m^2.
- Advanced colorectal cancer: Delay next dose until neutrophils recover to ≥1500/mm^3 and platelets recover to ≥75,000/mm^3, then reduce dose to 65 mg/m^2.

-Pulmonary toxicity (unexplained respiratory symptoms including nonproductive cough, dyspnea, crackles, pulmonary infiltrates): Discontinue until interstitial lung disease or pulmonary fibrosis have been excluded.

Common side effect:

- Central nervous system: Fatigue (61%), fever (25%), pain (14%), headache (13%), insomnia (11%)
- Gastrointestinal: Nausea (64%), diarrhea (46%), vomiting (37%), abdominal pain (31%), constipation (31%), anorexia (20%), stomatitis (14%)
- Hematologic: Anemia (64%; grades 3/4: 1%), thrombocytopenia (30%; grades 3/4: 3%), leukopenia (13%)
- Hepatic: AST increased (54%; grades 3/4: 4%), ALT increased (36%; grades 3/4: 1%), total bilirubin increased (13%; grades 3/4: 5%)
- Neuromuscular & skeletal: Peripheral neuropathy (may be dose limiting; 76%; acute 65%; grades 3/4: 5%; persistent 43%; grades 3/4: 3%), back pain (11%)
- Respiratory: Dyspnea (13%), cough (11%)

Pregnancy Risk Factor: D