# Oxator™ for IV Injection

Oxaliplatin for Injection USP

## DESCRIPTION

**Oxator™** is a preparation of Oxaliplatin. Oxaliplatin undergoes nonenzymatic conversion in physiologic solutions to active derivatives via displacement of the labile oxalate ligand. Several transient reactive species are formed, including monoaquo and diaquo DACH platinum, which covalently bind with macromolecules. Both inter-and intrastrand Pt-DNA crosslinks are formed. Crosslinks are formed between the N7 positions of two adjacent guanines (GG), adjacent adenine-guanines (AG), and guanines separated by an intervening nucleotide (GNG). These crosslinks inhibit DNA replication and transcription. Cytotoxicity is cell-cycle nonspecific.

## INDICATIONS

Oxaliplatin is a platinum-based drug used in combination with infusional 5-Fluorouracil/ Leucovorin, which is indicated for:

- Adjuvant treatment of stage III colon cancer in patients who have undergone complete resection of the primary tumor.
- Treatment of advanced colorectal cancer.

## DOSAGE AND ADMINISTRATION

» Administer Oxaliplatin in combination with 5-Fluorouracil/Leucovorin every 2 weeks.

**Day 1:** Oxaliplatin 85 mg/m$^2$ intravenous infusion in 250-500 mL 5% Dextrose Injection, and Leucovorin 200 mg/m$^2$ intravenous infusion in 5% Dextrose Injection, both given over 120 minutes at the same time in separate bags using a Y-line, followed by 5-Fluorouracil 400 mg/m$^2$ intravenous bolus given over 2-4 minutes, followed by 5-Fluorouracil 600 mg/m$^2$ intravenous infusion in 500 mL 5% Dextrose Injection, (recommended) as a 22-hour continuous infusion.

**Day 2:** Leucovorin 200 mg/m$^2$ intravenous infusion over 120 minutes, followed by 5-Fluorouracil 400 mg/m$^2$ IV bolus given over 2-4 minutes, followed by 5-Fluorouracil 600 mg/m$^2$ intravenous infusion in 500 mL 5% Dextrose Injection, (recommended) as a 22-hour continuous infusion.

» Reduce the dose of Oxaliplatin to 75 mg/m$^2$ (adjuvant setting) or 65 mg/m$^2$ (advanced colorectal cancer).

- If there are persistent grade 2 neurosensory events that do not resolve.
- After recovery from grade 3/4 gastrointestinal toxicities (despite prophylactic treatment) or grade 4 neutropenia or grade 3/4 thrombocytopenia. Delay next dose until neutrophils ≥1.5 x 10$^9$/L and platelets ≥75 x 10$^9$/L.

» For patients with severe renal impairment (creatinine clearance <30 mL/min), the initial recommended dose is 65 mg/m$^2$.

» Discontinue Oxaliplatin if there are persistent Grade 3 neurosensory events.

» Never reconstitute or prepare final dilution with a sodium chloride solution or other chloride-containing solutions.

## CONTRAINDICATIONS

- Hypersensitivity

## SIDE EFFECTS

- Peripheral sensory neuropathy
- Neutropenia, thrombocytopenia, anemia
- Nausea, diarrhea, stomatitis
- Increase in transaminases and alkaline phosphatase
- Fatigue
- Emesis

## WARNING AND PRECAUTION

- Allergic Reactions: Monitor for development of rash, urticaria, erythema, pruritis, bronchospasm, and hypotension.
- Neuropathy: Reduce the dose or discontinue Oxaliplatin if necessary.
- Pulmonary Toxicity: May need to discontinue Oxaliplatin until interstitial lung disease or pulmonary fibrosis are excluded.
- Hepatotoxicity: Monitor liver function tests.
- Pregnancy: Fetal harm can occur when administered to a pregnant woman. Women should be apprised of the potential harm to the fetus.

## USE IN PREGNANCY AND LACTATION

Pregnancy Category D. Oxaliplatin may cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies of Oxaliplatin in pregnant women. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Oxaliplatin.

It is not known whether Oxaliplatin or its derivatives are excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Oxaliplatin, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

## DRUG INTERACTIONS

No specific cytochrome P-450-based drug interaction studies have been conducted. No pharmacokinetic interaction between 85 mg/m$^2$ Oxaliplatin and 5-Fluorouracil/ Leucovorin has been observed in patients treated every 2 weeks. Increases of 5-Fluorouracil plasma concentrations by approximately 20% have been observed with doses of 130 mg/m$^2$ Oxaliplatin dosed every 3 weeks. Because platinum-containing species are eliminated primarily through the kidney, clearance of these products may be decreased by co-administration of potentially nephrotoxic compounds; although, this has not been specifically studied.

## INSTRUCTION FOR RECONSTITUTION AND FURTHER DILUTION

Reconstitution or final dilution must never be performed with a sodium chloride solution or other chloride containing solutions. The lyophilized powder is reconstituted by adding 10 mL (for the 50 mg vial) or 20 mL (for the 100 mg vial) of Water for Injection or 5% Dextrose Injection. Do not administer the reconstituted solution without further dilution. The reconstituted solution must be further diluted in an infusion solution of 250-500 mL of 5% Dextrose Injection.

Oxaliplatin is incompatible in solution with alkaline medications or media (such as basic solutions of 5-Fluorouracil) and must not be mixed with these or administered simultaneously through the same infusion line. The infusion line should be flushed with 5% Dextrose Injection prior to administration of any concomitant medication.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration and discarded if present. Needles or intravenous administration sets containing aluminum parts that may come in contact with Oxaliplatin should not be used for the preparation or mixing of the drug. Aluminum has been reported to cause degradation of platinum compounds.

## STORAGE AFTER RECONSTITUTION

After reconstitution in the original vial, the solution may be stored up to 24 hours under refrigeration [2-8 °C (36-46 °F)]. After final dilution with 250-500 mL of 5% Dextrose Injection, the shelf life is 6 hours at room temperature [20-25 °C (68-77 °F)] or up to 24 hours under refrigeration [2-8 °C (36-46 °F)]. Oxaliplatin is not light sensitive.

## HANDLING AND DISPOSAL

As with other potentially toxic anticancer agents, care should be exercised in the handling and preparation of infusion solutions prepared from Oxaliplatin. The use of gloves is recommended. If a solution of Oxaliplatin contacts the skin, wash the skin immediately and thoroughly with soap and water. If Oxaliplatin contacts the mucous membranes, flush thoroughly with water.

## PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light & wet place. Keep out of reach of children.

## PACKAGING

**Oxator™ 50 for IV Injection:** Each box contains 1 vial of Oxaliplatin USP 50 mg (as lyophilized powder).

**Oxator™ 100 for IV Injection:** Each box contains 1 vial of Oxaliplatin USP 100 mg (as lyophilized powder).

SK+F ONCOLOGY

Manufactured by
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