

Arixatin

Oxaliplatin BP

COMPOSITION

Arixatin 50 Concentrated Solution for IV Infusion: Each vial contains Oxaliplatin BP 50 mg as 10 ml concentrated solution for IV infusion.

Arixatin 100 Concentrated Solution for IV Infusion: Each vial contains Oxaliplatin BP 100 mg as 20 ml concentrated solution for IV infusion.

CLINICAL PHARMACOLOGY

Mechanism of action: Arixatin (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 adenineguanines (AG), and guanines separated by an intervening nucleotide (GNG). These crosslinks inhibit DNA replication and transcription. Cytotoxicity is cell-cycle nonspecific.

INDICATIONS

Arixatin Injection is a platinum-based drug used in combination with infusional fluorouracil and leucovorin, which applies to the following indications:

- 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

Day 1: Administration of Arixatin Injection 85 mg/m² as an intravenous infusion over 120 minutes and leucovorin 200 mg/m² as an intravenous infusion over 120 minutes at the same time in separate bags, followed by fluorouracil 400 mg/m² as intravenous bolus over 2 to 4 minutes, followed by fluorouracil 600 mg/m² as a 22-hour continuous infusion.

Day 2: Administration of leucovorin 200 mg/m² as an intravenous infusion over 120 minutes, followed by fluorouracil 400mg/m² as intravenous bolus over 2 to 4 minutes, followed by fluorouracil 600 mg/m² as a 22-hour continuous infusion.

Reduction of the dose of Oxaliplatin Injection may be required

- 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 febrile neutropenia or Grade 3/4 thrombocytopenia.

The dose for adjuvant setting will be 75 mg/m² and 65 mg/m² for advanced colorectal cancer. The next dose will be delayed until neutrophils become $\geq 1.5 \times 10^9/l$ and platelets $\geq 75 \times 10^9/l$.

Important Dosing Considerations

For patients with severe renal impairment (creatinine clearance < 30 ml/min), the initial recommended dose is 65 mg/m². Oxaliplatin Injection will be discontinued if there are persistent Grade 3 neurosensory events.

Dosage Modifications for Adjuvant Treatment in Patients with Stage III Colon Cancer

Adverse Reactions	Severity	Oxaliplatin Injection Dosage Modifications
Peripheral Sensory Neuropathy	Persistent Grade 2	Reduction of Oxaliplatin Injection dose to 75 mg/m ² should be considered
	Persistent Grade 3	Discontinuing of Oxaliplatin Injection should be considered
	Grade 4	Oxaliplatin Injection should be discontinued
Myelosuppression	Grade 4 neutropenia or febrile neutropenia	The next dose will be delayed until neutrophils $\geq 1.5 \times 10^9/l$ and platelets $\geq 75 \times 10^9/l$. Oxaliplatin Injection dose will be reduced to 75 mg/m ²
	Grade 3-4 thrombocytopenia	
Gastrointestinal Adverse Reactions	Grade 3-4	After recovery, Oxaliplatin Injection dose will be reduced to 75 mg/m ² along with a dose reduction of fluorouracil to 300 mg/m ² as an intravenous bolus and 500 mg/m ² as a 22-hour continuous infusion.

Dosage modifications for adverse reactions for advanced colorectal cancer

Adverse Reactions	Severity	Oxaliplatin Injection Dosage Modifications
Peripheral Sensory Neuropathy	Persistent Grade 2	Reduction of Oxaliplatin Injection dose to 65 mg/m ² should be considered
	Persistent Grade 3	Discontinuing of Oxaliplatin Injection should be considered
	Grade 4	Oxaliplatin Injection should be discontinued
Myelosuppression	Grade 4 neutropenia or febrile neutropenia	The next dose will be delayed until neutrophils $\geq 1.5 \times 10^9/l$ and platelets $\geq 75 \times 10^9/l$. Oxaliplatin Injection dose will be reduced to 65 mg/m ²
	Grade 3-4 thrombocytopenia	
Gastrointestinal Adverse Reactions	Grade 3-4	After recovery, Oxaliplatin Injection dose will be reduced to 65 mg/m ² along with a dose reduction of fluorouracil to 300 mg/m ² as an intravenous bolus and 500 mg/m ² as a 22-hour continuous infusion

Dose Modifications for Patients with Renal Impairment

In patients with severe renal impairment (creatinine clearance [CLCr] less than 30 ml/min.), reduction of the Oxaliplatin Injection dose to 65 mg/m².

PREPARATION AND ADMINISTRATION

Oxaliplatin Injection is a cytotoxic drug. Special handling and disposal procedures should be applicable as follows: The concentrated solution will be diluted with 250 to 500 ml of 5% Dextrose Injection. The diluted solution should not be stored for longer than 6 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 24 hours under refrigeration (2°C to 8°C [36°F to 46°F]). Visual inspection is required for particulate matter and discoloration prior to administration and discard if present. Dilution with sodium chloride solution or other chloride-containing solutions must not be performed. Alkaline medications or media (such as basic solutions of fluorouracil) should not be mixed with Oxaliplatin Injection or administered through the same infusion line concurrently. The infusion line should be flushed with 5% Dextrose Injection, prior to administration of any concomitant medication. Intravenous administration sets or needles containing aluminum parts should not be used for the preparation or mixing of Oxaliplatin Injection. Aluminum has been reported to cause degradation of platinum compounds.

ADVERSE EFFECTS

The most common adverse reactions (incidence $\geq 40\%$) are peripheral sensory neuropathy, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue and stomatitis

WARNINGS AND PRECAUTIONS

- Allergic Reactions:** Monitor for development of rash, urticaria, erythema, pruritus, bronchospasm, and hypotension.
- Neuropathy:** Reduce the dose or discontinue Oxaliplatin Injection if necessary.
- Severe Neutropenia:** Delay Oxaliplatin Injection until neutrophils are $\geq 1.5 \times 10^9/l$. Withhold Oxaliplatin Injection for sepsis.
- Pulmonary Toxicity:** May need to discontinue Oxaliplatin injection until interstitial lung disease or pulmonary fibrosis are excluded.
- Hepatotoxicity:** Monitor liver function tests.
- Cardiovascular Toxicity:** Correct hypokalemia or hypomagnesemia prior to initiating Oxaliplatin Injection.
- Rhabdomyolysis:** Discontinue Oxaliplatin Injection if rhabdomyolysis occurs.
- Embryo-Fetal Toxicity:** Can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise males and females of reproductive potential to use an effective method of contraception.

USE IN SPECIFIC POPULATION

Pregnancy: Based on direct interaction with DNA, Oxaliplatin Injection can cause fetal harm when administered to a pregnant woman

Nursing mothers: Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with Oxaliplatin Injection and for 3 months after the final dose.

Pediatric use: The effectiveness of Oxaliplatin Injection in children has not been established.

Geriatric use: No significant effect of age on the clearance of ultrafilterable platinum has been observed.

Females and Males of Reproductive Potential: Based on animal studies, Oxaliplatin Injection may impair fertility in males and females.

DRUG INTERACTIONS

No specific cytochrome P-450-based drug interaction studies have been conducted.

OVERDOSE

There is no known antidote for Oxaliplatin overdose. Patients suspected of receiving an overdose should be monitored, and supportive treatment should be administered. In addition to thrombocytopenia, the anticipated complications of an Oxaliplatin overdose include hypersensitivity reaction, myelosuppression, nausea, vomiting, diarrhea and neurotoxicity.

STORAGE

Store below 25° C. Keep in a dry place away from light. Keep out of the reach of children.

PRESENTATION

Arixatin 50 Concentrated Solution for IV Infusion: Each box contains 1 vial of Oxaliplatin BP 50 mg.

Arixatin 100 Concentrated Solution for IV Infusion: Each box contains 1 vial of Oxaliplatin BP 100 mg, one IV infusion set (with butterfly needle), one disposable syringe (10 ml), one alcohol pad and one first aid bandage.

Manufactured by:



ARISTOPHARMA LTD.

Shampur-Kadamtali I/A, Dhaka-Bangladesh

by Techno Drugs Ltd., Satirpara, Narsingdi.

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