Only for the use of a Registered Medical Practitioner or a Hospital or a Laboratory.

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Oxaliplatin for Injection USP

Lyophilised

XTIDE® 50 /100

LYxÉOÉCQ 50/100

XTIDE® 50
Each vial contains
Oxaliplatin USP 50 mg
Lactose Monohydrate q.s.
Reconstitute to 10ml with Sterile Water for Injections use immediately after preparation.

XTIDE® 100
Each vial contains
Oxaliplatin USP 100 mg
Lactose Monohydrate q.s.
Reconstitute to 20ml with Sterile Water for Injections use immediately after preparation.

Do not inject without prior dilution.
For Intravenous infusion only.

FORM
Lyophilised powder for infusion

COMPOSITION
Each vial contains:

Active Ingredients	XTIDE™ 50	XTIDE™ 100
Oxaliplatin USP	50 mg	100 mg
Lactose Monohydrate	450 mg	900 mg

DESCRIPTION
Oxaliplatin for injection is an antineoplastic agent. It is an organoplatinum complex in which the platinum atom is complexed with 1,2-diaminocyclohexane (DACH) and with an oxalate ligand as a leaving group.

CLINICAL PHARMACOLOGY
MECHANISM OF ACTION
Oxaliplatin undergoes non enzymatic 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 cross links are formed. Cross links are formed between the N7 positions of two adjacent guanines (CG), adjacent adenine-guanine (AG) and guanines separated by an intervening nucleotide (GNG). These cross links inhibit DNA replication and transcription. Cytotoxicity is cell-cycle nonspecific.

PHARMACOKINETIC
After intravenous administration, Oxaliplatin is widely distributed throughout the body. It binds irreversibly to red blood cells, which can prolong the half-life of the drug. The mean terminal half-life is 273 hours.

Oxaliplatin is extensively metabolized to both inactive and active compounds and is predominantly excreted in the urine.

INDICATIONS AND USAGE
Oxaliplatin is indicated for the treatment of advanced colorectal cancer.

DOSAGE AND ADMINISTRATION
Adjuvant Therapy in Patients with Stage III Colon Cancer
Adjuvant treatment in patients with stage III colon cancer is recommended for a total of 6 months, i.e., 12 cycles, every 2 weeks, according to the dose schedule.

Therapy in Previously Untreated and Previously Treated Patients with Advanced Colorectal Cancer

The recommended dose schedule to be given every two weeks is as follows:
Day 1: Oxaliplatin 85mg/m^2 IV infusion in 250-500mL D5W and Leucovorin 200mg/m^2 IV infusion in D5W both given over 120 minutes at the same time in separate bags using a T-line, followed by 5-FU 400mg/m^2 IV bolus given over 2-4 minutes, followed by 5-FU 600mg/m^2 IV infusion in 500 D5W (recommended) as a 22-hour continuous infusion.
Day 2: Leucovorin 200mg/m^2 IV infusion over 120 minutes, followed by 5-FU 400mg/m^2 bolus given over 2-4 minutes, followed by 5-FU 600mg/m^2 IV infusion in 500mL D5W (recommended) as a 22-hour continuous infusion.

Repeat cycle every 2 weeks
The administration of Oxaliplatin does not require prehydration.

Dose Modification Recommendations
As peripheral neuropathy is the dose limiting toxicity, following dose adjustments have to be made when occurs:
- If symptoms last longer than 7 days are troublesome, the subsequent dose of Oxaliplatin should be reduced by 25%
- If paraesthesia persists until the next cycle, the subsequent dose of Oxaliplatin should be reduced by 25%
- Oxaliplatin should be discontinued if troublesome paraesthesia or functional impairment persists until the next cycle.
- Resumption of therapy should be considered if these symptoms improve following discontinuation of Oxaliplatin.

When Oxaliplatin is combined with fluorouracil, the usual dose adjustments for 5-fluorocil associated toxicities should apply.

Preparation of Infusion Solution
Reconstitution or final dilution must never be performed with a sodium chloride solution or other chloride-containing solutions.

The lyophilised powder is reconstituted by adding 10 mL (for the 50 mg vial) or 20 mL (for the 100 mg vial) of water for injection, USP or 5% Dextrose injection, USP. Do not administer the reconstituted solution without further dilution. The reconstituted solution must be further diluted in an infusion of 250-500 mL of 5% Dextrose injection, USP.

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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, USP, 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)].

OVERDOSAGE
There is no known antidote for Oxaliplatin overdosage. In general, supportive care and frequent monitoring of vital signs should be administered.

CONTRAINDICATION
Oxaliplatin should not be administered to patients with a history of known allergy to Oxaliplatin or other platinum compounds.

Drug - Drug Interaction
No Pharmacokinetics interaction between 85 mg/m^2 of Oxaliplatin for injection and infusion 5-FU has been observed in patients treated every 2 weeks, but increases of 5-FU plasma concentrations by approximately 20% have been observed with doses of 130 mg/m^2 of Oxaliplatin for injection administrated every 3 weeks.

PRECAUTIONS
Oxaliplatin should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents.

Pulmonary Toxicity
Oxaliplatin for injection has been associated with pulmonary fibrosis (< 1% of study patients), which may be fatal. The combined incidence of cough and dyspnea was 7.4% (any grade) and <1% (grade 3) with no grade 4 events in the Oxaliplatin plus infusional 5-FU/LV arm compared arm compared to 4.5% (any grade) and no grade 3 and 0.1% grade 4 events in the influsional 5-FU/LV alone arm in adjuvant colon cancer patients.

Hepatotoxicity
In adjuvant study, hepatotoxicity was observed more commonly in Oxaliplatin combination arm with increase in transaminases (57% vs 34%) and alkaline phosphatase (42% vs 20%).

Use in Pregnant and Lactating Women
Safety and efficacy has not been established in pregnant and lactating women. Therefore it is not recommended for use in pregnant and lactating women.

ADVERSE REACTIONS
The most common adverse reaction in patients with stage II or III colon cancer receiving adjuvant therapy, were peripheral sensory neuropathy, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue and stomatitis.

Oxaliplatin is not light sensitive.

Oxaliplatin is incompatible in solution with alkaline medications or media (such as basic solutions of 5-FU) and must not be mixed with these or administrated simultaneously through the same infusion line. The infusion line should be flushed with 5DW 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.

INFORMATION FOR PATIENTS
Patients and patient's caregivers should be informed of the expected side effects of Oxaliplatin for injection, particularly its neurologic effects, both the acute, reversible effects and the persistent neurosensory toxicity. Patients should be informed that the acute neurosensory toxicity may be precipitated or exacerbated by exposure to cold or cold objects. Patients should be instructed to avoid cold drinks, use of ice, and should cover exposed skin prior to exposure to cold temperature or cold objects.

STORAGE
Store below 25°C. Do not freeze.
Keep out of the reach of children.

PRESENTATION
Oxaliplatin for injection is available as single use vial containing Lyophilised powder of Oxaliplatin 50 mg/vial and 100 mg/vial.

For further details, please contact:
Biocon Limited
20th KM, Hosur oad,
Electronics City,
Bangalore - 560 100. India

1104742/DS460

To report adverse events and/or product complaints visit our website www.biocon.com or call toll free No: 1800 102 9465 or e mail us at drugsafety@Biocon.com

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