Oxalipaltin Injection

COMPOSITION

Zolon 50 & 100 (25 ml & 50 ml Vial)

Each ml contains:

Oxaliplatin BP.....2 mg

Zolon 150

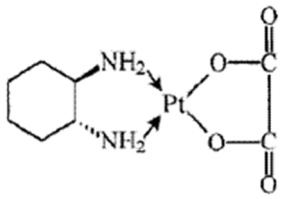
Each ml contains:

Oxalipaltin BP.....5 mg

DESCRIPTION

Oxalipaltin a cell cycle –phase monspecific antineoplastic drugs belongs to a new class of platinum agent that contains a platinum atom complexed with oxalate and diaminocyclothexane (DACH.)

CHEMICAL STRUCTURE



Chemically Oxaliplatin is trans -l – diaminocyclothexane oxatatoplatinum or cis –(oxalate(trans –(1.2, -diamino-cyclothexane) platinum (III) . The empirical formula of Oxaliplatin is $C_2H_4N_2O_4Pt$. The molecular weight of Oxaliplatin is 397.30. Oxaliplatin is slightly soluble in water and methanol , and insoluble in ehanol.

CLINICAL PHARMACOLOGY
MECHANISM OF ACTION

The exact mechanism of action of Oxaliplatin is not known. The mechanism of action of Oxaliplatin is probably similar to that of cisplatin. Oxaliplatin forms reactive platinum complexes that are believed to inhbit DNA synthesis by forming intrastrand cross-linking of DNA molecules. Oxaliplatin is not cross

resistant to cisplatin or carboplatin. Probably due to the DACH group and resistance to DNA mismatch repair Oxaliplatin is a radiation sensitizing agent.

PHARMACOKINETICS

After intravenous distribution. Oxalipaltin is mainly accumulated in erythrocytes and dose not diffuse in to the plasma 85-88 % of platinum is protein bound in the first 5 hours after administration. Oxaliplatin undergoes rapid nonezymatic biotransformation to reactive platinum complexes. The active metabolites of oxaliplatin are DACH platinum species. Oxaliplatin is excreted mainly by renal excretion. Approximately 50% of the administered dose is excreted in the urine within the first 3 days. Fecal excretion is approximately 0.5%per day and reaches 5% of the total dose by day 11. The terminal half – life of ultra filterable platinum (Oxaliplatin and free Oxaliplatin metabolites) is 283± 19 hrs. The platinum elimination from the erythrocytes takes about 48 days.

INDICATIONS

Oxaliplatin is indicated in the treatment of metastatic colorectal cancers after failure of treatment of fluoropyrimidines , alone by monochemotherapy or along with fluoropyrimidines.

DOSAGE AND ADMINISTRATION:

Colorectal Cancer In Adults

- As single agent:
- When used alone, the recommended dose of Oxaliplatin is 130mg/m^2 as a continuous intravenous infusion over 2 to 6 hours. The dose may be repeated at an interval of 3 weeks.
- In combination therapy:
- IV : On day 1 : administer oxaliplatin 85 mg/m^2 concurrently with leucovorin 200mg/m^2 (in separate containers using a Y line) by IV infusion over 2 hours. Then administer fluorouracil 400mg/m^2 by IV injection over 2 to 4 minutes, followed by fluorouracil 500mg/m^2 by IV infusion over 22 hours

- On day 2 – administer leucovorin 200mg/m^2 by IV infusion over 2 hours. Then administer fluorouracil 400 mg/m^2 by IV injection over 2 to 4 minutes, followed by fluorouracil 600 mg/m^2 by IV infusion over 22 hours. Repeat regimen at intervals of 2 weeks

Dosage adjustment in toxicity

Symptom	Oxaliplatin dose	Fluorouracil & Leucovorin
Peripheral neuropathy	Administer over 6 hours	No adjustment required

Persistent grade 2 neurosensory effect	Reduce dose by 25% (i.e. 65mg/m)	No adjustment required
In patients who recover from grade 3 or 4 GI toxicity grade 4 neutropenia or grade 3 or 4 thrombocy topenia	Reduce dose by 25% (i.e. 65mg/m)	Reduce fluorouracil dose by 20% (i.e. to 300mg/m^2 by IV injection over 2 to 4 minutes and 500 mg/m^2 by IV infusion over 22 hours

- Do not administer next dose until neutrophilcourt > 1500/mm^2 and platelet count > 75.000m^2

Renal Impairment:

In patients with impaired renal function, observed caution

MONITORING PRAMETERS:

Assess the patients for differential WBC count, hemoglobin, Platelet count, and ALT, AST, bilirubin and creatinine level before each Oxaliplatin cycle.

WARNING

- Oxaliplatin should be administered under the supervision of qualified physician experienced in the use of cancer chemotherapeutic agents.
- Aluminum has been reported to cause degradation of platinum compounds and hence needles of intravenous administration sets containing aluminum parts that may come in contact with oxaliplatin should not be used for the preparation or mixing of the drugs.
- Oxaliplatin should not be administered undiluted. Dilute with 5% Dextrose infusion.
- Oxaliplatin is incompatible in solution with alkaline medications or media and hence it is advised that oxaliplatin should never be diluted with Sodium Chloride/Chloride – containing infusion solutions.
- Oxaliplatin has been found to be mutagenic in mammalian in vitro mutation chromosome test. Although carcinogenic studies have not been done. Oxaliplatin is considered a probable carcinogen.
- Oxaliplatin is embryotoxic and fetotoxic in rates. Oxaliplatin may cause fetal harm when administered to pregnant women. The patient should be apprised of the potential hazard to the fetus and potential risk for loss of the pregnancy if there is exposure to Oxaliplatin during pregnancy.

PRECAUTIONS

- Oxaliplatin should not be mixed with any other medication and it should not be administered simultaneously by the same infusion line.
- Caution is recommended while administering Oxaliplatin to patients with known hypersensitivity to other platinum agents.
- It is known whether oxaliplatin is excreted in human milk or not caution should be exercised when oxaliplatin is administered to a nursing woman as many drugs are excreted in human milk.
- Inspect the solution visually for particulate matter and discoloration prior to administration.

ADVERSE REACTION

Commonly occurring adverse effect of Oxaliplatin are:

- Sensory neuropathy
- Anemia
- Fever
- Nausea & Vomiting
- Liver function abnormalities
- Infections
- Alopecia
- Pharyngolaryngeal dysesthesia

Other side effects that become more pronounced when used in combination with flurouracil and leucovorin are:

- Neutropenia
- Thrombocytopenia
- Diarrhorea
- Mucostitis

DRUG INTERRACTION

Oxaliplatin induces irinotecan related cholinergic syndrome by potentiating irinotecan inhibition of acetylcholinesterase. Oxaliplatin has no influence on flurouracil and topotecan pharmacokinetics. Preclinical studies have shown oxaliplatin to be synergetic with flurourocil and SN-38, the active metabolite of irinotican.

There are no other studies documenting any major intractions of oxalipaltin with other drugs.

OVERDOSAGE:

There is no know antidote for Oxaliplatin overdosage in general supportive care and frequent monitoring of vital signs should be administered

CONTRAINDICATIONS

Oxaliplatin is contraindicated in patient with

- History of severe allergy to the drug
- Severe Pre-existing peripheral neuropathy
- Severe rena dysfunction (Crcl<30ml/min)
- Pregnancy and Breast feeding

STORAGE:

To be stored at a temperature below 25°C. Protect from light. Do not freeze

PRESENTATION

Zolon as 25ml vial- containing 50 mg of oxaliplatin

Zolon as 50ml vial- containing 100 mg of oxaliplatin.

Zolon as 30ml vial- containing 50 mg of oxaliplatin.

Manufactured in India by:

ZUVIUS LIFESCIENCES PVT. LTD.
A WHO-GMP CERTIFIED COMPANY
B/111, 112, 113, Kanara Business Centre,
Link Road, Ghatkopar (East), Mumbai 400075.
www.zuviuslifesciences.in