

Xaloplat

Oxaliplatin



COMPOSITION

Xaloplat Aqua 50 Injection: Each vial contains Oxaliplatin BP 50 mg (5mg/mL).
Xaloplat Aqua 100 Injection: Each vial contains Oxaliplatin BP 100 mg (5mg/mL).
Xaloplat Aqua 200 Injection: Each vial contains Oxaliplatin BP 200 mg (5mg/mL).

DESCRIPTION

Xaloplat Aqua is a clear, colorless solution, free from visible particles.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Oxaliplatin is an antineoplastic drug belonging to a new class of platinum based compounds in which the platinum atom is complexed with 1, 2-diaminocyclohexane (DACH) and an oxalate group. Oxaliplatin is a single enantiomer, the cis-(oxalato) (trans-1, 2- DACH) platinum.

Oxaliplatin exhibits a wide spectrum of both in vitro cytotoxicity and in vivo antitumor activity in a variety of tumour model systems, including human colorectal cancer models. Oxaliplatin also demonstrates in vitro and in vivo activity in various cisplatin resistant models.

A synergistic cytotoxic action has been observed in combination with fluorouracil both in vitro and in vivo.

Studies on the mechanism of action of oxaliplatin, although not completely elucidated, show that the aqua-derivatives resulting from the biotransformation of oxaliplatin interact with DNA to form both inter- and intra-strand cross links, resulting in the disruption of DNA synthesis leading to cytotoxic and antitumor effects.

Pharmacokinetics

At the end of a two hour infusion, 15% of the administered platinum is present in the systemic circulation, the remaining 85% being rapidly distributed into tissues or eliminated in the urine. Irreversible binding to red blood cells and plasma results in half-lives in these matrices that are close to the natural turnover of red blood cells and serum albumin. No accumulation was observed in plasma ultrafiltrate following 85 mg/m² every two weeks or 130 mg/m² every three weeks and steady-state was attained by cycle one in this matrix. Inter- and intra-subject variability is generally low. Biotransformation in vitro is considered to be the result of non-enzymatic degradation and there is no evidence of cytochrome P450 mediated metabolism of the diaminocyclohexane (DACH) ring.

Oxaliplatin undergoes extensive biotransformation in patients, and no intact drug was detectable in plasma ultrafiltrate at the end of a two hour infusion. Several cytotoxic biotransformation products including the monochloro, dichloro and diaquo DACH platinum species have been identified in the systemic circulation together with a number of inactive conjugates at later time points.

Platinum is predominantly excreted in urine, with clearance mainly in the 48 hours following administration. By day 5, approximately 54% of the total dose was recovered in the urine and <3% in the faeces. A significant decrease in clearance of ultrafiltrable platinum from 17.6 ± 2.18 L/hour to 9.95 ± 1.91 L/hour in renal impairment (creatinine clearance 12- 57 mL/minute) was observed together with a statistically significant decrease in distribution volume from 330 ± 40.9 to 241 ± 36.1 L. The effect of severe renal impairment on platinum clearance has not been evaluated.

INDICATIONS

Oxaliplatin, in combination with fluorouracil and folinic acid, is indicated for:

- Adjuvant treatment of stage III (Duke's C) colon cancer after complete resection of the primary tumour
- Treatment of advanced colorectal cancer.

DOSE AND ADMINISTRATION

Dosage

In combination with fluorouracil and folinic acid the recommended dose for the treatment of advanced colorectal cancer is 85 mg/m² intravenously repeated every two weeks, or 130mg/m² repeated every three weeks.

In combination with fluorouracil and folinic acid the recommended dose for adjuvant treatment is 85 mg/m² intravenously repeated every two weeks for 12 cycles (6 months).

Dosage Modification

Prior to each treatment cycle, patients should be evaluated for toxicity and the dose of oxaliplatin adjusted accordingly.

Neurological Toxicity

If acute neurological reactions occur eg acute pharyngolaryngeal dysaesthesia, increase the oxaliplatin infusion time from 2 hours to 6 hours. This decreases Cmax by 30% and may lessen acute toxicities.

If sensory loss or paraesthesia persists longer than 7 days or interferes with function (grade 2 toxicity), reduce oxaliplatin dose by 25%.

If sensory loss or paraesthesia interferes with activities of daily living (grade 3 toxicity), oxaliplatin should be discontinued.

Haematological Toxicity

If haematological toxicity (neutrophils < 1.5 x 10⁹/L or platelets < 75 x 10⁹/L) is present before starting treatment or prior to the next course:

- Delay treatment until neutrophil count is 1.5 x 10⁹/L and platelet count is 75 x 10⁹/L and
 - Reduce the 85mg/m² oxaliplatin dose to 75mg/m² every two weeks and FU dose by 20% (adjuvant treatment)
 - Reduce the 85mg/m² oxaliplatin dose to 65mg/m² every two weeks and FU dose by 20% (advanced treatment)
 - Reduce the 130mg/m² oxaliplatin dose to 100mg/m² every three weeks and FU dose by 20% (advanced treatment)

Gastrointestinal Toxicity

If grade 3-4 gastrointestinal reactions occur, as assessed according to US National Cancer Institute criteria:

- Delay treatment until resolution of the adverse reactions and

- Reduce the 85mg/m² oxaliplatin dose to 75mg/m² every two weeks and FU dose by 20% (adjuvant treatment)
- Reduce the 85mg/m² oxaliplatin dose to 65mg/m² every two weeks and FU dose by 20% (advanced treatment)
- Reduce the 130mg/m² oxaliplatin dose to 100mg/m² every three weeks and FU dose by 20% (advanced treatment).

Toxicity associated with fluorouracil

Dose adjustments should also be made for fluorouracil associated toxicities (see relevant product information).

Oxaliplatin should be administered before fluorouracil.

Oxaliplatin is administered as a 2- to 6-hour intravenous infusion in 250 to 500 mL of 5% glucose injection.

Preparation and Administration

- Oxaliplatin is a cytotoxic drug. Follow applicable special handling and disposal procedures.
- Do not freeze.
- Protect the concentrated solution from light.
- Dilute concentrated solution with 250 to 500 mL of 5% Dextrose Injection, USP. Do not dilute with sodium chloride solution or other chloride-containing solutions.
- Store diluted solution for no more 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)). Protection from light is not required.
- Visually inspect for particulate matter and discoloration prior to administration and discard if present.
- Do not mix Oxaliplatin or administer Oxaliplatin through the same infusion line concurrently with alkaline medications or media (such as basic solutions of fluorouracil).
- Flush the infusion line with 5% Dextrose Injection, USP prior to administration of any concomitant medication.
- Do not use needles or intravenous administration sets containing aluminum parts for the preparation or mixing of Oxaliplatin. Aluminum has been reported to cause degradation of platinum compounds.
- Administer Oxaliplatin as an intravenous infusion over 120 minutes concurrently with leucovorin over 120 minutes in separate bags.

Dilution before Infusion

The solution MUST be further diluted in an infusion solution of 250-500 mL of 5% glucose injection. From a microbiological and chemical point of view, this infusion preparation should be used immediately. Inspect visually prior to use. Only clear solutions without particles should be used. The product is for single use in one patient only. Discard any residue. NEVER use sodium chloride solution for either reconstitution or dilution.

Oxaliplatin diluted in 250 to 500 mL of a glucose 5% injection must be infused either by central venous line or peripheral vein over 2 to 6 hours. When oxaliplatin is administered with fluorouracil, the oxaliplatin infusion should precede that of fluorouracil.

Oxaliplatin can be co-administered with folinic acid infusion using a Y-tube placed immediately before the site of injection. The drugs should not be combined in the same infusion bag. Folinic acid must be diluted using isotonic infusion solutions such as 5% glucose solution but NOT sodium chloride solutions or alkaline solutions.

Flush the line after oxaliplatin administration. While oxaliplatin has minimal to no vesicant potential, extravasation may result in local pain and inflammation which may be severe and lead to complications especially when oxaliplatin is infused through a peripheral vein. In case of oxaliplatin extravasation, the infusion must be stopped immediately and the usual local symptomatic treatment initiated.

Disposal

Oxaliplatin is a cytotoxic drug. Follow applicable special handling and disposal procedures. 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.

CONTRAINDICATIONS

Known allergy to oxaliplatin or other platinum compounds.

PRECAUTIONS

General

Oxaliplatin should be administered only by or under the supervision of an experienced clinical oncologist.

Allergic Reactions

Anaphylactic-like reactions to oxaliplatin have been reported, and may occur within minutes of oxaliplatin administration. Patients with a history of allergic reactions to platinum compounds should be monitored for allergic symptoms. In case of an anaphylactic type reaction to oxaliplatin, the infusion should be immediately discontinued and appropriate symptomatic treatment initiated. Rechallenge with oxaliplatin is contraindicated.

Neurological Toxicity

Neurological toxicity of oxaliplatin should be carefully monitored, especially if co-administered with other medications with specific neurological toxicity. A neurological examination should be performed before initiation of each administration, and periodically thereafter. It is not known whether patients with pre-existing medical conditions associated with peripheral nerve damage have a reduced threshold for oxaliplatin induced peripheral neuropathy.

For patients who develop acute laryngopharyngeal dysaesthesia, during or within 48 hours following the two hour infusion, the next oxaliplatin infusion should be administered over six hours. To prevent such dysaesthesia, advise the patient to avoid exposure to cold and to avoid ingesting cold food and/or beverages during or within 48 hours following oxaliplatin administration.

Gastrointestinal Toxicity

Gastrointestinal toxicity, which manifests as nausea and vomiting, warrants prophylactic antiemetic therapy, including 5-HT₃-antagonists and corticosteroids. Dehydration, ileus, intestinal obstruction, hypokalaemia, metabolic acidosis and renal impairment may be caused by severe diarrhoea/ emesis, particularly when combining oxaliplatin with fluorouracil.

Haematological Toxicity

Monitor haematological toxicity with a full blood count and white cell differential count prior to starting therapy and before each subsequent course. Idiosyncratic haematological toxicity may occur, especially in patients who have received previous myelotoxic treatment.

Pulmonary Toxicity

Oxaliplatin has been associated with pulmonary fibrosis (0.7% of study patients), which may be fatal. In the case of unexplained respiratory symptoms such as non-productive cough, dyspnoea, crackles or radiological pulmonary infiltrates, oxaliplatin should be discontinued until further pulmonary investigations exclude an interstitial lung disease or pulmonary fibrosis.

Hepatic Toxicity

Reactions related to liver sinusoidal obstruction syndrome, including nodular regenerative hyperplasia, have been reported. In the case of abnormal liver function test results or portal hypertension which could not be explained by liver metastases, reactions related to liver sinusoidal obstruction syndrome should be investigated, and very rare cases of drug induced hepatic vascular disorders should be considered.

Renal Impairment

Oxaliplatin has not been studied in patients with severe renal impairment. It is therefore contraindicated in patients with severe renal impairment.

There is limited information on safety in patients with moderately impaired renal function, and administration should only be considered after suitable appraisal of the benefit/ risk for the patient. However, treatment may be initiated at the normally recommended dose. In this situation, renal function should be closely monitored and dose adjusted according to toxicity.

There is no need for dose adjustment in patients with mild renal dysfunction.

Hepatic Insufficiency

Oxaliplatin has not been studied in patients with severe hepatic impairment. No increase in oxaliplatin acute toxicities was observed in the subset of patients with abnormal liver function tests at baseline. No specific dose adjustment for patients with abnormal liver function tests was performed during clinical development.

Carcinogenicity, Mutagenicity and Effects on Fertility

Oxaliplatin was shown to be mutagenic and clastogenic in mammalian test systems in vitro and in vivo. The carcinogenic potential of oxaliplatin has not been studied, but compounds with similar mechanisms of action and genotoxicity profiles have been reported to be carcinogenic. Oxaliplatin should be considered a probable carcinogen.

In dogs dosed with oxaliplatin, a decrease in testicular weight accompanied with testicular hypoplasia approaching aplasia was seen at doses 15 mg/m². However, no effects on fertility were seen in male and female rats at doses up to 12 mg/m²/day for five days per cycle.

ADVERSE EFFECTS

Most common adverse reactions (incidence > 40%) were peripheral sensory neuropathy, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue and stomatitis. Other adverse reactions, including serious adverse reactions, have been reported.

USE IN PREGNANCY (CATEGORY D)

Reproductive toxicity studies showed no teratogenic activity in rats or rabbits at intravenous doses up to 6 and 9 mg/m² /day respectively (1/20 of the maximum recommended clinical dose, based on body surface area). However, increased embryonic deaths, decreased foetal weight and delayed ossifications were observed in rats. Related compounds with similar mechanisms of action have been reported to be teratogenic. There are no adequate and well controlled studies in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the foetus. Oxaliplatin is probably toxic to the human foetus at the recommended therapeutic dose, and is therefore contraindicated during pregnancy.

As with other cytotoxic agents, effective contraceptive measures should be taken in potentially fertile patients prior to initiating chemotherapy with oxaliplatin.

Use in Lactation

There are no data on the excretion of oxaliplatin into milk of animals or humans. Oxaliplatin is contraindicated in breastfeeding women.

Paediatric Use

Oxaliplatin is not recommended for use in children as safety and efficacy have not been established in this group of patients.

Use in the Elderly

No increase in severe toxicities was observed when oxaliplatin was given as a single agent or in combination with fluorouracil in patients over the age of 65. In consequence no specific dose adaptation is required for elderly patients.

DRUG INTERACTIONS

In patients who have received a single dose of 85 mg/m² of oxaliplatin, immediately before administration of fluorouracil, no change in the level of exposure to fluorouracil has been observed. However, in patients dosed with fluorouracil weekly and oxaliplatin 130 mg/m² every 3 weeks, increases of 20% in fluorouracil plasma concentrations have been observed.

In vitro little or no displacement of oxaliplatin binding to plasma proteins has been observed with the following agents: erythromycin, salicylates, griseofulvin, paclitaxel and sodium valproate.

Oxaliplatin is incompatible with chloride containing solutions and basic solutions (including fluorouracil), therefore oxaliplatin should not be mixed with these or administered simultaneously via the same intravenous line. There are no data for compatibility with other drugs.

The lack of cytochrome P450 mediated metabolism indicates that oxaliplatin is unlikely to modulate the P450 metabolism of concomitant medications through a competitive mechanism.

OVERDOSE

There is no known antidote for Oxaliplatin overdose. In addition to thrombocytopenia, the anticipated complications of an Oxaliplatin overdose include hypersensitivity reaction, myelosuppression, nausea, vomiting, diarrhea and neurotoxicity.

Several cases of overdoses have been reported with Oxaliplatin. Adverse reactions observed were Grade 4 thrombocytopenia (<25,000/mm³) without any bleeding, anemia, sensory neuropathy such as paresthesia, dyesthesia, laryngospasm and facial muscle spasms, gastrointestinal disorders such as nausea, vomiting, stomatitis, flatulence, abdomen enlarged and Grade 4 intestinal obstruction, Grade 4 dehydration, dyspnea, wheezing, chest pain, respiratory failure, severe bradycardia and death.

Patients suspected of receiving an overdose should be monitored, and supportive treatment should be administered. The maximum dose of oxaliplatin that has been administered in a single infusion is 825 mg.

PHARMACEUTICAL INFORMATION

Storage Condition

Store the vial in original carton below 25°C. Protect from light. Do not freeze. Keep out of the reach of the children.

Packaging

Xaloplat Aqua 50 Injection: Each commercial box contains 1 vial of Oxaliplatin BP 50 mg.

Xaloplat Aqua 100 Injection: Each commercial box contains 1 vial of Oxaliplatin BP 100 mg.

Xaloplat Aqua 200 Injection: Each commercial box contains 1 vial of Oxaliplatin BP 200 mg.

জেলোপ্লাট

অক্সালিপ্লাটিন



উপাদানঃ

জেলোপ্লাট অ্যাকুয়া ৫০ ইনজেকশনঃ

প্রতি ভায়ালে থাকে অক্সালিপ্লাটিন বিপি ৫০ মিগ্রা (৫মিগ্রা/মিলি)।

জেলোপ্লাট অ্যাকুয়া ১০০ ইনজেকশনঃ

প্রতি ভায়ালে থাকে অক্সালিপ্লাটিন বিপি ১০০ মিগ্রা (৫মিগ্রা/মিলি)।

জেলোপ্লাট অ্যাকুয়া ২০০ ইনজেকশনঃ

প্রতি ভায়ালে থাকে অক্সালিপ্লাটিন বিপি ২০০ মিগ্রা (৫মিগ্রা/মিলি)।

বর্ণনাঃ

জেলোপ্লাট অ্যাকুয়া পরিষ্কার, বর্ণহীন, কলিকাহীন দ্রব।

ট্রিনিকাল ফার্মাকোলজিঃ

ফার্মাকোকাইনেটিক্সঃ

অক্সালিপ্লাটিন একটি anti neoplastic গুণ্ডু এবং একটি নতুন শ্রেণির প্রাটিনাম মুক্ত বৌয়ের অর্ধায়ু যথেষ্ট প্রাটিনাম অণু ১, ২- diaminocyclohexane এবং অক্সালেটের সাথে জটিল অণু গঠন করে।

অক্সালিপ্লাটিন বিস্তার পরিসরে ইন ভিত্রো সাইটোটক্সিসিটি এবং ইন ভিভো টিউমার প্রতিরোধী সক্রিয়তা প্রদর্শন করে।

ফার্মাকোকাইনেটিক্সঃ

দুই ঘণ্টার ইনফিউশনের পরে, ১৫% প্রাটিনাম সিস্টেমিক সার্ভুলেশনে এবং বাকি ৮৫% প্রাটিনাম টিস্যুতে অথবা মূত্রে সাথে অপসারিত হয়।

নন এনজাইমেটিক জড়নের মাধ্যমে ইন ভিত্রো বায়োট্রান্সফরমেশনে ঘটে।

প্রাটিনাম মূলত মূত্রের মাধ্যমে অপসারিত হয় এবং এই অপসারণ হয় গুণ্ডু প্রয়োগের ৪৮ ঘণ্টার মধ্যে।

নির্দেশনাঃ

১। স্টেজ ৩ (Duke's C) কোলন ক্যান্সারের সহায়ক চিকিৎসায়, প্রাথমিক টিউমারের সম্পূর্ণ অপসারণের পর

২। অ্যাডভান্সড কোলোরেক্টাল ক্যান্সারের চিকিৎসায়

মাত্রা ও সেবনবিধিঃ

অ্যাডভান্সড কোলোরেক্টাল ক্যান্সারের চিকিৎসায় ফ্লুরোইউরাসিল এবং ফলিনিক এসিডের সাথে অক্সালিপ্লাটিনের নির্দেশিত সেবনমাত্রা ৮৫ মিগ্রা/মি^২ intravenously প্রতি দুই সপ্তাহে পুনরাবৃত্তি করতে হবে, অথবা ১০০ মিগ্রা/ মি^২ প্রতি তিন সপ্তাহে পুনরাবৃত্তি করতে হবে।

ফ্লুরোইউরাসিল এবং ফলিনিক এসিডের সাথে সহায়ক হিসেবে অক্সালিপ্লাটিনের নির্দেশিত সেবনমাত্রা ৮৫ মিগ্রা/মি^২ intravenously প্রতি দুই সপ্তাহে পুনরাবৃত্তি করতে হবে ১২ সাইকেলের জন্য (৬ মাস)।

সেবনমাত্রা পরিবর্তনঃ

প্রতি সাইকেলের আগে টক্সিসিটি এবং সেবনমাত্রা মন্যায়ণ করতে হবে এবং সেবনমাত্রা সেবনমাত্রা সে অনুযায়ী পরিবর্তন করতে হবে।

প্রতিনির্দেশনাঃ

অক্সালিপ্লাটিন বা অন্য প্রাটিনাম বৌশো আবার্জ

সতর্কতা ও সাবধানতাঃ

সাধারণঃ

কেবলমাত্র অভিজ্ঞ ট্রিনিকাল অনকোলজিস্টের তত্ত্বাবধানে অক্সালিপ্লাটিন দ্বারা চিকিৎসা গ্রহণ করতে হবে।

অ্যাডভার্সিক প্রতিক্রিয়াঃ

অক্সালিপ্লাটিনে আনানকাইসোটিক জাতীয় প্রতিক্রিয়ার প্রথম পাণ্ডা গিয়েছে এবং এটি অক্সালিপ্লাটিন প্রদানের কয়েক মিনিটের মধ্যে হতে পারে। সেসব রোগীর প্রাটিনাম দ্বারা আবার্জের ইতিহাস আছে তাদের ক্ষেত্রে আবার্জিক লক্ষণ পর্যবেক্ষণ করতে হবে। যাদের ক্ষেত্রে অক্সালিপ্লাটিনে দ্বারা আনানকাইসোটিক প্রতিক্রিয়া দেখা যায়, তাদের ক্ষেত্রে ইনফিউশন বন্ধ করতে হবে এবং লক্ষণগুলোর যথাযথ চিকিৎসা নিতে হবে।

নিউরোলজিক্যাল টক্সিসিটিঃ

অক্সালিপ্লাটিন দ্বারা নিউরোলজিক্যাল টক্সিসিটি সতর্কতার সাথে পর্যবেক্ষণ করতে হবে, বিশেষ করে সেসব গুণ্ডুদের নিউরোলজিক্যাল টক্সিসিটি প্রদর্শন করে তাদের সাথে সেবনের সময়। অক্সালিপ্লাটিন দ্বারা চিকিৎসার পূর্বে নিউরোলজিক্যাল পরীক্ষা করতে হবে।

গ্যাস্ট্রোইন্টেস্টাইনাল টক্সিসিটিঃ

গ্যাস্ট্রোইন্টেস্টাইনাল টক্সিসিটি যেমন বমিভাব, বমির জন্য চিকিৎসার পূর্বে বমিরোধক গুণ্ডু, 5-HT₃ antagonists এবং কটিকোটেরয়েড প্রয়োগ করতে হবে।

হেপাটোলজিক্যাল টক্সিসিটিঃ

চিকিৎসা শুরু পূর্বে শ্বেতকণিকা এবং সম্পূর্ণ বাড কাউন্ট সম্পূর্ণভাবে এবং প্রত্যেক কোর্সের পূর্বে পর্যবেক্ষণ করতে হবে।

পালমোনারি টক্সিসিটিঃ

অক্সালিপ্লাটিন পালমোনারি টক্সিসিটির সাথে সম্পর্কিত (০.৭% রোগীর ক্ষেত্রে) যা মারাত্মক হতে পারে।

হেপাটিক টক্সিসিটিঃ

নিজস্ব সাইনুসয়ডাল অবস্ট্রাকশন সিনড্রোম যেমন, নতুনকার রিক্রোনোটিক হাইপারপ্লাসিয়ার রিপোর্ট করা হয়েছে।

সেবনমাত্রা পরিবর্তনঃ

সেবনমাত্রা পরিবর্তনঃ

সেবনবিধিঃ

সেবনবিধিঃ

সেবনবিধিঃ

সেবনবিধিঃ

সেবনবিধিঃ

সেবনবিধিঃ

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সেবনবিধিঃ

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