ONCOLOGY

Oxaliplatin Kabi 5 mg/ml

Trusted Generics: Total Care

Oxaliplatin Kabi 5 mg/ml
concentrate for solution for infusion

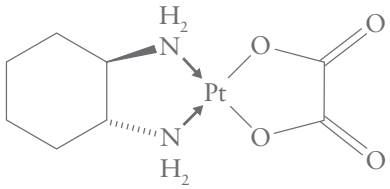
FRESENIUS KABI

caring for life

Oxaliplatin Kabi liquid

Therapeutic class

Platinium analog



Indications

Oxaliplatin Kabi in combination with 5-fluorouracil (5FU) and folinic acid (FA) is indicated for:

- Adjuvant treatment of stage III (Duke's C) colon cancer after complete resection of primary tumor
- Treatment of metastatic colorectal cancer

The colour of the packaging is designed to improve patient and user safety and to distinguish between different products in our range.

Oxaliplatin Kabi liquid is available as follows:

	50 mg	10 ml	Vial
	100 mg	20 ml	Vial
	200 mg	40 ml	Vial
Composition	1 ml of concentrate for solution for infusion contains 5 mg oxaliplatin		
Pharmaceutical form	Concentrate for solution for infusion, clear, colourless liquid		
Excipients	Succinic acid, sodium hydroxide and water for injections		
Shelf life	3 years (before opening the vial)		

Oxaliplatin Kabi in focus

- Cell cycle non-specific cytotoxic agent
- Exerts its anti-tumor activity on cancerous cells, throughout their life cycle
- Proven survival benefits in colorectal cancers

Stability

The unopened vials of Oxaliplatin Kabi injection are stable until the date indicated on the package when stored under recommended storage condition in the original package. Solution for infusion prepared as recommended are stable at ambient temperature (approx. 25°C).

Additional stability information is available from your local Fresenius Kabi representative.

Compatibility

Solution should be prepared in glass, polyethylene or polypropylene containers.

Manufacturing and safety

Oxaliplatin Kabi is made by Fresenius Kabi from our own raw materials, giving us full control of the manufacturing and supply chain*. Our state of the art cleaning process for finished vials guarantees the removal of all external contamination.

Fresenius Kabi sleeved vials (OncoShield®) offers maximum protection for people working with cytotoxic drugs.

* The source of active pharmaceutical ingredient may vary in different countries.

Abridged SPC of Oxaliplatin Kabi 5 mg/ml Concentrate for Solution for Infusion (Oxaliplatin)

Composition: 1 ml of concentrate for solution for infusion contains 5 mg Oxaliplatin. 10 ml of concentrate for solution for infusion contains 50 mg of Oxaliplatin. 20 ml of concentrate for solution for infusion contains 100 mg of Oxaliplatin. **Therapeutic indications:** Oxaliplatin in combination with 5-fluorouracil (5FU) and folinic acid (FA) is indicated for: Adjuvant treatment of stage III (Duke's C) colon cancer after complete resection of primary tumor. Treatment of metastatic colorectal cancer. **Posology and method of administration:** Posology: For adults only: The recommended dose for Oxaliplatin in adjuvant setting is 85 mg/m^2 intravenously repeated every two weeks for 12 cycles (6 months). The recommended dose for Oxaliplatin in treatment of metastatic colorectal cancer is 85 mg/m^2 intravenously repeated every 2 weeks. Dosage given should be adjusted according to tolerability. **Oxaliplatin should always be administered before fluoropyrimidines, i.e. 5-fluorouracil (5FU).** Oxaliplatin is administered as a 2- to 6-hour intravenous infusion in 250 to 500 ml of glucose 5% solution to give a concentration between 0.20 mg/ml and 0.70 mg/ml; 0.70 mg/ml is the highest concentration in clinical practice for an Oxaliplatin dose of 85 mg/m^2. Oxaliplatin has mainly been used in combination with continuous infusion 5-fluorouracil based regimens. For the two-weekly treatment schedule 5-fluorouracil regimens combining bolus and continuous infusion were used. Special Populations: *Renal impairment:* Oxaliplatin has not been studied in patients with severe renal impairment. In patients with moderate renal impairment, treatment may be initiated at the normally recommended dose. There is no need for dose adjustment in patients with mild renal dysfunction. *Hepatic insufficiency:* In a phase I study including patients with several levels of hepatic impairment, frequency and severity of hepato-biliary disorders appeared to be related to progressive disease and impaired liver function tests at baseline. No specific dose adjustment for patients with abnormal liver function tests was performed during clinical development. *Elderly patients:* No increase in severe toxicities was observed when Oxaliplatin was used as a single agent or in combination with 5-fluorouracil in patients over the age of 65. In consequence no specific dose adaptation is required for elderly patients. Method of administration: Oxaliplatin is administered by intravenous infusion. The administration of Oxaliplatin does not require hyperhydration. Oxaliplatin diluted in 250 to 500 ml of glucose 5 % solution to give a concentration not less than 0.20 mg/ml must be infused via a central venous line or a peripheral vein over 2 to 6 hours. Oxaliplatin infusion must always precede the administration of 5-fluorouracil. In the event of extravasation, administration must be discontinued immediately. Instructions for use: Oxaliplatin must be diluted before use. Only glucose 5% diluent is to be used to dilute the concentrated solution for infusion. **Contraindications:** Oxaliplatin is contraindicated in patients who have a known history of hypersensitivity to Oxaliplatin, are breast feeding, have myelosuppression prior to starting first course, as evidenced by baseline neutrophils $< 2 \times 109/l$ and/or platelet count of $< 100 \times 109/l$, have a peripheral sensory neuropathy with functional impairment prior to first course, have a severely impaired renal function (creatinine clearance less than 30 ml/min). **Special warnings and precautions for use:** Oxaliplatin should only be used in specialised departments of oncology and should be administered under the supervision of an experienced oncologist. Due to limited information on safety in patients with moderately impaired renal function, administration should only be considered after suitable appraisal of the benefit/risk for the patient. In this situation, renal function should be closely monitored and dose adjusted according to toxicity. Patients with a history of allergic reaction to platinum compounds should be monitored for allergic symptoms. In case of an anaphylactic-like reaction to Oxaliplatin, the infusion should be immediately discontinued and appropriate symptomatic treatment initiated. Oxaliplatin rechallenge is contra-indicated. In case of Oxaliplatin extravasation, the infusion must be stopped immediately and usual local symptomatic treatment initiated. Neurological toxicity of Oxaliplatin should be carefully monitored, especially if co-administered with other medicinal products with specific neurological toxicity. A neurological examination should be performed before each administration and periodically thereafter. For patients who develop acute laryngopharyngeal dysaesthesia, during or within the hours following the 2-hour infusion, the next Oxaliplatin infusion should be administered over 6 hours. If neurological symptoms (paraesthesia, dysaesthesia) occur, the following recommended Oxaliplatin dosage adjustment should be based on the duration and severity of these symptoms. If symptoms last longer than seven days and are troublesome, the subsequent Oxaliplatin dose should be reduced from 85 mg/m^2 to 65 mg/m^2 (metastatic setting) or 75 mg/m^2 (adjuvant setting). If paraesthesia without functional impairment persists until the next cycle, the subsequent Oxaliplatin dose should be reduced from 85 mg/m^2 to 65 mg/m^2 (metastatic setting) or 75 mg/m^2 (adjuvant setting). If paraesthesia with functional impairment persists until the next cycle, Oxaliplatin should be discontinued. If these symptoms improve following discontinuation of Oxaliplatin therapy, resumption of therapy may be considered. Patients should be informed of the possibility of persistent symptoms of peripheral sensory neuropathy after the end of the treatment. Localized moderate paresthesias or paresthesias that may interfere with functional activities can persist after up to 3 years following treatment cessation in the adjuvant setting. Gastrointestinal toxicity, which manifests as nausea and vomiting, warrants prophylactic and/or therapeutic antiemetic therapy. Dehydration, paralytic ileus, intestinal obstruction, hypokalemia, metabolic acidosis and renal impairment may be caused by severe diarrhoea/emesis particularly when combining Oxaliplatin with 5-fluorouracil. If haematological toxicity occurs (neutrophils $< 1.5 \times 109/l$ or platelets $< 50 \times 109/l$), administration of the next course of therapy should be postponed until haematological values return to acceptable levels. A full blood count with white cell differential should be performed prior to start of therapy and before each subsequent course. Patients must be adequately informed of the risk of diarrhoea/emesis, mucositis/stomatitis and neutropenia after Oxaliplatin/5-fluorouracil administration so that they can urgently contact their treating physician for appropriate management. If mucositis/stomatitis occurs with or without neutropenia, the next treatment should be delayed until recovery from mucositis/stomatitis to grade 1 or less and/or until the neutrophil count is $\geq 1.5 \times 109/l$. For Oxaliplatin combined with 5-fluorouracil (with or without folinic acid), the usual dose adjustments for 5-fluorouracil associated toxicities should apply. If grade 4 diarrhoea, grade 3–4 neutropenia (neutrophils<1.0x109/l), grade 3 to 4 thrombocytopenia (platelets $< 50 \times 109/l$) occur, the dose of Oxaliplatin should be reduced from 85 mg/m^2 to 65 mg/m^2 (metastatic setting) or 75 mg/m^2 (adjuvant setting), in addition to any 5-fluorouracil dose reductions required. 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 (see section 4.8). In case of abnormal liver function test results or portal hypertension, which does not obviously result from liver metastases, very rare cases of drug-induced hepatic vascular disorders should be considered. Genotoxic effects were observed with Oxaliplatin in the preclinical studies. Therefore male patients treated with Oxaliplatin are advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment because Oxaliplatin may have an anti-fertility effect, which could be irreversible. Women should not become pregnant during treatment with Oxaliplatin and should use an effective method of contraception. **Interaction with other medicinal products and other forms of Interaction:** *In vitro,* no significant displacement of Oxaliplatin binding to plasma proteins has been observed with the following agents: erythromycin, salicylates, granisetron, paclitaxel, and sodium valproate. **Pregnancy and lactation:** To date there is no available information on safety of use in pregnant women. In animal studies, reproductive toxicity was observed. Consequently, Oxaliplatin is not recommended during pregnancy and in women of childbearing potential not using contraceptive measures. The use of Oxaliplatin should only be considered after suitably appraising the patient of the risk to the foetus and with the patient's consent. Appropriate contraceptive measures must be taken during and after cessation of therapy during 4 months for women and 6 months for men. Excretion in breast milk has not been studied. Breast-feeding is contra-indicated during Oxaliplatin therapy. Oxaliplatin may have an anti-fertility effect. **Effects on ability to drive and use machines:** No studies on the effects on the ability to drive and use machines have been performed. However Oxaliplatin treatment resulting in an increase risk of dizziness, nausea and vomiting, and other neurologic symptoms that affect gait and balance may lead to a minor or moderate influence on the ability to drive and use machines. **Undesirable effects:** The most frequent adverse events of Oxaliplatin in combination with 5-fluorouracil/folinic acid (5FU/FA), were gastrointestinal (diarrhoea, nausea, vomiting and mucositis), haematological (neutropenia, thrombocytopenia) and neurological (acute and dose cumulative peripheral sensory neuropathy). Overall, these events were more frequent and severe with Oxaliplatin and 5FU/FA) combination than with 5FU/FA alone. **Overdose:** There is no known antidote to Oxaliplatin. In cases of overdose, exacerbation of adverse events can be expected. Monitoring of haematological parameters should be initiated and symptomatic treatment given. **List of excipients:** Succinic acid, sodium hydroxide and water for injections. **Shelf life:** 2 years. After dilution in glucose 5% solution, chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15°C to 25°C) and at refrigerated condition (2 °C to 8 °C). From a microbiological point of view, the solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C unless dilution has taken place in controlled and validated aseptic conditions. **Special precautions for storage:** Do not freeze. Store below 30 °C. Keep the vial in the outer carton in order to protect from light.

Registered product information may differ in your country. Before prescribing refer to nationally approved Prescribing Information. Before prescribing please refer to nationally registered and approved Summary of Product Characteristics.

FRESENIUS KABI

caring for life

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