

Package leaflet: Information for the user
Oxaliplatin 5 mg/ml concentrate for solution for infusion
Oxaliplatin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Oxaliplatin is and what it is used for
2. What you need to know before you use Oxaliplatin
3. How to use Oxaliplatin
4. Possible side effects
5. How to store Oxaliplatin
6. Contents of the pack and other information

1. What Oxaliplatin is and what it is used for

The active ingredient of oxaliplatin concentrate for solution for infusion is oxaliplatin. Oxaliplatin is an anti-cancer drug and is used to treat metastatic (advanced) cancer of the colon (large bowel) or rectum (back passage), or as additional treatment following surgery to remove a tumour (growth) in the colon. It is used in combination with other anti-cancer medicines called 5-fluorouracil (5-FU) and folinic acid (FA).

2. What you need to know before you use Oxaliplatin

Do not use Oxaliplatin:

- if you are allergic to Oxaliplatin or any of the other ingredients of this medicine (listed in section 6).
- if you are breastfeeding
- if you already have a reduced number of blood cells.
- if you already have tingling and numbness in the fingers and/or toes, and have difficulty performing delicate tasks, such as buttoning clothes
- if you have a severe kidney problem.

Warnings and precautions

Talk to your doctor or pharmacist or nurse before using Oxaliplatin

- if you have mild or moderate kidney problems.
- if you have ever suffered an allergic reaction to other platinum-containing medicines such as carboplatin or cisplatin.
- if you have symptoms of nerve damage such as weakness, numbness, disturbance of feeling after previous oxaliplatin treatment. These effects are often triggered by exposure to cold. If you notice such symptoms tell your doctor, especially if they are troublesome and/or last longer than 7 days. Your doctor will regularly carry out neurological examinations, before and regularly during treatment, especially if you are given other drugs which may cause nerve damage.
- if you have any liver problems.
- if your blood cell counts are too low after previous infusions of oxaliplatin. Your doctor will regularly take blood to check you have sufficient blood cells.

Before and/or during treatment with oxaliplatin you may be given special medicinal products to prevent and/or treat vomiting.

Children

Oxaliplatin should not be given to children.

Other medicines and Oxaliplatin

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

Pregnancy

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

You must not become pregnant during treatment with oxaliplatin and must use an effective method of contraception. If pregnancy occurs during your treatment, you must immediately inform your doctor. You should take appropriate

contraceptive measures during and after cessation of therapy continuing for 4 months for women and 6 months for men.

Breast-feeding

You must not breast-feed while you are treated with oxaliplatin.

Fertility

Oxaliplatin may have an anti-fertility effect, which could be irreversible. Male patients are therefore 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. Male patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 6 months.

Driving and using machines:

Oxaliplatin treatment may result in an increased risk of dizziness, nausea and vomiting, and other neurologic symptoms that affect gait and balance. If this happens, you should not drive or operate machinery.

3. How to use Oxaliplatin

Oxaliplatin is intended only for adults.

Dosage

The dose of Oxaliplatin is based on your body surface area (calculated by m²).This is calculated from your height, weight and your state of health. It also depends on other medicines that are used in your cancer treatment.

The usual dose for adults including the elderly is 85 mg/m² of body surface area once every 2 weeks, before the infusion of the other anti-cancer medicines.

The dose you receive will also depend on results of blood tests and whether you have previously experienced side effects with Oxaliplatin.

Method and route of administration

- Oxaliplatin will be prescribed for you by a specialist in cancer treatment.
- You will be treated by a healthcare professional, who will have made up the required dose of Oxaliplatin.
- Oxaliplatin is diluted before being given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period.
- The needle must remain in the vein while the drug is being given. If the needle comes out or becomes loose, or the solution is going into the tissue outside the vein (you may feel discomfort or pain) - **tell the doctor or nurse immediately.**

Frequency of administration

You should usually receive your infusion once every 2 weeks.

Duration of treatment

The duration of treatment will be determined by your doctor. Your treatment will last a maximum of 6 months when used after complete resection of your tumour.

If you are given more Oxaliplatin than you should

As this medicine is administered by a healthcare professional, it is highly unlikely that you will be given too little or too much. In case of overdose, you may experience increased side effects. Your doctor may give you appropriate treatment for these side effects.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you experience any side effect it is important that you inform your doctor before your next treatment.

You will find described below the side effects that you could experience.

Tell your doctor immediately if you notice any of the following:

Symptoms of an allergic or anaphylactic reaction with sudden signs such as rash, itching or hives on the skin, difficulties in swallowing, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing, extreme tiredness (you may feel you are going to faint). **In the majority of cases, these symptoms occurred during the infusion or immediately after but delayed allergic reactions have also been observed hours or even days after the infusion.**

- Abnormal bruising, bleeding or signs of infection such as a sore throat and high temperature,
- Persistent or severe diarrhoea or vomiting,
- Stomatitis/mucositis (sore lips or mouth ulcers),

The following information is intended for healthcare professionals only:

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

As with other potentially toxic compounds, caution should be exercised when handling and preparing oxaliplatin solutions.

Instructions for Handling

The handling of this cytotoxic agent by healthcare personnel requires every precaution to guarantee the protection of the handler and his surroundings.

The preparations of injectable solutions of cytotoxic agents must be carried out by trained specialist personnel with knowledge of the medicines used, in conditions that guarantee the integrity of the medicinal product, the protection of the environment and in particular the protection of the personnel handling the medicines, in accordance with the hospital policy. It requires a preparation area reserved for this purpose. It is forbidden to smoke, eat or drink in this area.

Personnel must be provided with appropriate handling materials, notably long sleeved gowns, protection masks, caps, protective goggles, sterile single-use gloves, protective covers for the work area, containers and collection bags for waste.

Faeces and vomit must be handled with care.

Pregnant women must be warned to avoid handling cytotoxic agents.

Any broken container must be treated with the same precautions and considered as contaminated waste. Contaminated waste should be incinerated in suitably labelled rigid containers. See below section "Disposal".

If oxaliplatin concentrate or solution for infusion, should come into contact with skin, wash immediately and thoroughly with water.

If oxaliplatin concentrate or solution for infusion, should come into contact with mucous membranes, wash immediately and thoroughly with water.

- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only glucose 5% infusion solution is to be used as a diluent. DO NOT dilute for infusion with sodium chloride or chloride containing solutions.
- DO NOT mix with any other drugs in the same infusion bag or administer simultaneously by the same infusion line.
- DO NOT mix with alkaline drugs or solutions, in particular 5 fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of other active substances. Alkaline medicinal products or solutions will adversely affect the stability of oxaliplatin.

Instruction for use with folinic acid (as calcium folinate or disodium folinate)

Oxaliplatin 85 mg/m² intravenous infusion in 250 to 500 ml of 5 % glucose solution is given at the same time as folinic acid intravenous infusion in 5 % glucose solution, over 2 to 6 hours, using a Y-line placed immediately before the site of infusion. These two drugs should not be combined in the same infusion bag. Folinic acid must not contain trometamol as an excipient and must only be diluted using isotonic 5 % glucose solution, never in alkaline solutions or sodium chloride or chloride containing solutions.

Instruction for use with 5 fluorouracil

Oxaliplatin should always be administered before fluoropyrimidines – i.e. 5 fluorouracil (5 FU). After oxaliplatin administration, flush the line and then administer 5 fluorouracil (5 FU).

For additional information on drugs combined with oxaliplatin, see the corresponding manufacturer's summary of product characteristics.

- USE ONLY the recommended solvents (see below).
- Any concentrate that shows evidence of precipitation should not be used and should be destroyed with due regard to legal requirements for disposal of hazardous waste (see below).

Concentrate for solution for infusion

Inspect visually prior to use. Only clear solutions without particles should be used. The medicinal product is for single use only. Any unused infusion solution should be discarded.

Dilution before intravenous infusion

Without the required amount of

- Unexplained respiratory symptoms such as a dry cough, difficulty in breathing or crackles,
- A group of symptoms such as extreme tiredness, little or infrequent urination and abnormal bleeding or bruising (signs of haemolytic uremic syndrome).

Other known side effects of Oxaliplatin are:

Very common: may affect more than 1 in 10 people

- A disorder of the nerves which can cause weakness, tingling or numbness in the fingers, toes, around the mouth or in the throat that may sometimes occur in association with cramps. This is often triggered by exposure to cold e.g. opening a refrigerator or holding a cold drink. You may also have difficulty in performing delicate tasks, such as buttoning clothes. Although in the majority of cases these symptoms resolve completely there is a possibility of persistent symptoms after the end of the treatment
- Oxaliplatin can sometimes cause an unpleasant sensation in the throat, in particular when swallowing, and give the sensation of shortness of breath. This sensation, if it happens, usually occurs during or within hours of the infusion and may be triggered by exposure to the cold. Although unpleasant, it will not last long and goes away without the need for any treatment. Your doctor may decide to alter your treatment as a result
- Signs of infection such as a sore throat and high temperature
- Reduction in the number of white blood cells, which make infections more likely
- Reduction in blood platelets, which increases risk of bleeding or bruising
- Reduction in red blood cells, which can make the skin pale and cause weakness or breathlessness. Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course
- Allergic reactions - skin rash including red itchy skin, swelling of the hands, feet, ankles, face, lips, mouth or

- throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint
- Loss or lack of appetite
- Too high levels of glucose (sugar) in your blood which may cause a great thirst, dry mouth or a need to urinate more often
- Low blood levels of potassium which can cause abnormal heart rhythm
- Low blood levels of sodium which can cause tiredness and confusion, muscle twitching, fits or coma
- Taste disorder
- Headache
- Nosebleeds
- Shortness of breath
- Coughing
- Nausea, vomiting - medication to prevent sickness is usually given to you by your doctor before treatment and may be continued after treatment.
- Diarrhoea, if you suffer from persistent or severe diarrhoea or vomiting contact your doctor immediately for advice.

- Sore mouth or lips, mouth ulcers
- Stomach pain, constipation
- Skin disorder
- Hair loss
- Back pain
- Tiredness, loss of strength/weakness, body pain
- Pain or redness close to or at the injection site during the infusion
- Fever which may be accompanied by shaking (rigors)
- Blood tests which show changes in the way the liver is working
- Weight gain (when oxaliplatin is used after surgery to remove the tumour)

Common: may affect up to 1 in 10 people

- Runny nose
- Nose and throat infection
- Dehydration
- Dizziness
- Inflammation of the nerves accompanied by pain, disturbances of feeling, reduced action of the nerve. Other symptoms of nerve disorders which have been reported include jaw or muscle spasms, twitching, muscle contractions, coordination and balance problems, staggering, double or abnormal/decreased vision, drooping of eyelids, voice problems (hoarseness or loss of voice), speech problems, abnormal tongue sensation, facial or eye pain
- Neck stiffness, intolerance/dislike of bright light and headache

- Conjunctivitis, visual problems
- Abnormal bleeding, blood in the urine, stools or vomit
- Blood clot, usually in a leg, which causes pain swelling or redness
- Blood clot in the lungs which causes chest pain and breathlessness
- Flushing
- Chest pain
- Hiccups
- Indigestion and heartburn
- Flaking skin, skin rash, increased sweating and nail disorder
- Joint pain and bone pain
- Pain on passing urine or a change in frequency when passing urine
- Abnormal blood tests which show worsening in the way the kidney is working
- Weight loss (when oxaliplatin is used in the treatment of advanced disease that has spread beyond the bowel to other tissues)
- Depression
- Difficulty sleeping
- Reduction in the number of a special form of white blood cells accompanied by
- fever and/or generalized infection
- Throat or chest tightness

Uncommon: may affect up to 1 in 100 people

- Blockage or swelling of the bowel
- Feeling anxious or nervous
- Hearing problems
- Blood tests which show an increase in the body’s acidity
- Temporary loss of vision.

Rare: may affect up to 1 in 1,000 people

- Deafness
- Slurred speech
- Scarring of the lungs which may cause shortness of breath and/or cough
- Bowel inflammation which causes abdominal pain and/or diarrhoea which may be bloody
- Inflammation of the optic nerve, visual field disturbances
- Reduction in red blood cells caused by cell destruction, and reduction in blood platelets due to an allergic reaction
- Inflammation of the pancreas
- A group of symptoms such as headache, dizziness, fits, high blood pressure and sight problems (signs of reversible posterior leukoencephalopathy syndrome).

Very rare: may affect up to 1 in 10,000 people

- Liver disease
- Kidney inflammation and kidney failure

Unknown: frequency cannot be estimated from the available data

- Allergic vasculitis (inflammation of blood vessels)
- Auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia).

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly:

For UK - via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

For Ireland - HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Oxaliplatin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after Exp. The expiry date refers to the last day of that month.

Keep the vial in the outer carton in order to protect from light. Store below 25°C. Do not freeze.

Do not use Oxaliplatin if you notice that the solution is not clear and free of particles.

concentrate from the vial(s) and then dilute with 250 ml to 500 ml of a 5% glucose solution to give an oxaliplatin concentration between 0.2 mg/ml and 0.7 mg/ml. The concentration range over which the physico-chemical stability of oxaliplatin has been demonstrated is 0.2 mg/ml to 2.0 mg/ml.

Administer by intravenous infusion. After dilution in 5% glucose solution, chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15°C -25°C) and at refrigerated condition (2°C -8°C).

From a microbiological point of view, this infusion preparation 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.

Inspect visually prior to use. Only clear solutions without particles should be used. The medicinal product is for single use only. Any unused infusion solution should be discarded.

NEVER use sodium chloride or chloride containing solutions for dilution.

The compatibility of Oxaliplatin solution for infusion has been tested with representative, PVC-based, administration sets.

Infusion

The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 to 500 ml of 5% glucose solution to give a concentration not less than 0.2 mg/ml must be infused either by peripheral vein or central venous line over 2 to 6 hours. When oxaliplatin is administered with 5-fluorouracil, the oxaliplatin infusion must precede the administration of 5-fluorouracil.

Disposal

Any unused medicinal product or waste material should be disposed

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment

6. Contents of the pack and other information

What Oxaliplatin contains:

- The active substance is Oxaliplatin. 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
 - 40 ml of concentrate for solution for infusion contains 200 mg of oxaliplatin
- The other ingredient is water for injections

What Oxaliplatin looks like and contents of the pack

This medicinal product is a concentrate for solution for infusion. It is a clear, colourless concentrate for solution for infusion free from visible particles.

Each vial contains 50 mg, 100 mg or 200 mg oxaliplatin. The concentrate is supplied in 10 ml, 20 ml and 40 ml concentrate in a Type I clear glass vial with chlorobutyl elastomer stopper and aluminium flip-off overseal. Each vial may be shrink wrapped and may/ may not be packed in a plastic container.

The vials are supplied in cartons of one vial.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

For UK:

Fresenius Kabi Oncology Plc.
Lion Court, Farnham Road, Bordon Hampshire, GU35 0NF
United Kingdom

For IRL :

Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.Höhe
Germany

Manufacturer:

Fresenius Kabi Oncology Plc.
Lion Court, Farnham Road
Bordon, Hampshire,
GU35 0NF United Kingdom

Fresenius Kabi Deutschland GmbH
Pflingstweide 53
61169 Friedberg
Germany

This medicinal product is authorised in the Member States of the EEA under the following names

Czech republic	Oxaliplatin Kabi 5 mg/ml koncentrát pro infuzní roztok
Denmark	Oxaliplatin "Fresenius Kabi", koncentrat til infusionsvæske, opløsning
Germany	Oxaliplatin Kabi 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Hungary	Oxaliplatin Kabi 5 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Oxaliplatin 5 mg/ml concentrate for solution for infusion
Italy	Oxaliplatino Kabi 5 mg/ml
Netherlands	Oxaliplatine Fresenius Kabi 5 mg/ml concentraat voor oplossing voor infusie
Norway	Oxaliplatin Fresenius Kabi 5 mg/ml koncentrat til infusjonsvæske
Poland	Oxaliplatin Kabi
Portugal	Oxaliplatina Kabi 5 mg/ml concentrado para solução para perfusão
Slovak republic	Oxaliplatin Kabi 5 mg/ml infúzny koncentrát
Spain	Oxaliplatino Kabi 5 mg/ml kconcentrado para solución para perfusión EFG
United Kingdom	Oxaliplatin 5 mg/ml concentrate for solution for infusion

The 5 mg/ml concentrate for solution for infusion was revised in February 2019