Package leaflet: Information for the user

Oxaliplatin 5 mg/ml
powder for solution for infusion

Oxaliplatin

Read all of this leaflet carefully before you start 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 or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

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 5 mg/ml powder for solution for infusion is oxaliplatin.

This medicine is used to treat cancer of the large bowel (treatment of stage III colon cancer after complete resection of primary tumour, metastatic cancer of colon and rectum). Oxaliplatin is used in combination with other anticancer medicines called 5-fluorouracil and folinic acid.

Oxaliplatin is an antineoplastic or anticancer drug and contains platinum.

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 breast-feeding.
- 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 severe kidney problems.

Warnings and precautions

Talk to your doctor or pharmacist before using Oxaliplatin
- If you have ever suffered an allergic reaction to platinum-containing medicines such as carboplatin, cisplatin. Allergic reactions can occur during any oxaliplatin infusion,
- If you have mild or moderate kidney problems.
- If you have any liver problems.

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.

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

It is not recommended that you become pregnant during treatment with oxaliplatin and must use an effective method of contraception. Female patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 4 months.

If you are pregnant or planning a pregnancy it is very important that you discuss this with your doctor before you receive any treatment.

If you get pregnant during your treatment, you must immediately inform your doctor.

Breast-feeding

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

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.

Driving and using machines

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

If you have vision problems while taking Oxaliplatin, do not drive, operate heavy machines or engage in dangerous activities.

3. How to use Oxaliplatin

Oxaliplatin is intended for adults only.

For single use only.

Dosage

The dose of oxaliplatin is based on your body surface area. This is calculated from your height and weight.

The usual dose for adults including the elderly is 85 mg/m² of body surface area. 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 given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period.
- Oxaliplatin will be given to you at the same time as folinic acid and before the infusion of 5 fluorouracil.

Frequency of administration

You should usually receive your infusion once every 2 weeks.

Duration of treatment

The duration of the 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 given in a hospital, it is 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, nurse or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everyone 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:
- Abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature,
- Persistent or severe diarrhoea or vomiting,
- Presence of blood or dark brown coffee-coloured particles in your vomit,
- Stomatitis/mucositis (sore lips or mouth ulcers),
- Unexplained respiratory symptoms such as dry cough, difficulties in breathing or crackles,
- A group of symptoms such as headache, altered mental functioning, seizures and abnormal vision from blurriness to vision loss (symptoms of reversible posterior leukoencephalopathy syndrome, a rare neurological disorder).

Other known side effects of oxaliplatin are:

Very common (affects more than 1 person in 10)
- Oxliplatin can affect the nerves (peripheral neuropathy). You may feel a tingling and/or numbness in the fingers, toes, around the mouth or in the throat, which may sometimes occur in association with cramps.

These effects are 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 themselves completely there is a possibility of persistent symptoms of peripheral sensory neuropathy after the end of the treatment.

Some people have experienced a tingling, shock-like sensation passing down the arms or trunk when the neck is flexed.
- 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.
- Oxaliplatin may cause diarrhoea, mild nausea (feeling sick) and vomiting (being sick); however medication to prevent the sickness is usually given to you by your doctor before treatment and may be continued after treatment.
- Oxaliplatin causes temporary reduction in the number of blood cells.
- The reduction of red cells may cause anaemia (a reduction of red cells), abnormal bleeding or bruising (due to a reduction in platelets).
  The reduction in white blood cells may make you prone to infections.

Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course.
- Sensation of discomfort close to or at the injection site during the infusion,
- Fever, rigors (tremors), mild or severe tiredness, body pain,
- Weight changes, loss or lack of appetite, taste disorders, constipation,
- Headache, back pain,
- Swelling of the nerves to your muscles, neck stiffness, abnormal tongue sensation possibly altering speech, stomatitis/mucositis (sore lips or mouth ulcers),
- Stomach pain,
- Abnormal bleeding including nose bleeds,
- Coughing, difficulty in breathing,
- Allergic reactions, skin rash which may be red and itchy, mild hair loss (alopecia),
- Alteration in blood tests including those relating to abnormalities in liver function.

Common (affects less than 1 person in 10)
- Infection due to a reduction in white blood cells,
- Indigestion and heart burn, hiccups, flushing, dizziness,
- Increased sweating and nail disorders, flaking skin,
- Chest pain,

The following information is intended for healthcare professionals only:

INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

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 preparation 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.

Excreta 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 chapter "Disposal".

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

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

Special precautions for administration
- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only glucose 5% (50 mg/ml) infusion solution is to be used as a diluent. DO NOT reconstitute or dilute for infusion with sodium chloride or chloride containing solutions.
- DO NOT mix with any other medicinal products 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 others active substances. Alkaline drugs 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 ml to 500 ml of glucose 5% (50 mg/ml) solution is given at the same time as folinic acid (FA) intravenous infusion in glucose 5% (50 mg/ml) solution, over 2 to 6 hours, using a Y-line placed immediately before the site of infusion.

These two medicinal products 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 glucose 5% (50 mg/ml) 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.

After oxaliplatin administration, flush the line and then administer 5-fluorouracil.

Any reconstituted solution which shows signs of precipitation may not be used and should be destroyed with due regard to legal requirements for disposal of hazardous waste.

Reconstitution of the solution
- Water for injection or 5% (50 mg/ml) glucose solution should be

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- Lung disorders and runny nose,
- Joint pain and bone pain,
- Pain on passing urine and changes in kidney function, changes of frequency of urination, dehydration,
- Blood in the urine/stools, swelling of the veins, clots in the lung,
- High blood pressure,
- Depression and insomnia,
- Conjunctivitis and visual problems.

Uncommon (affects less than 1 person in 100)

- Blockage or swelling of the bowel,
- Nervousness.

Rare (affects less than 1 person in 1000)

- Loss of hearing,
- Scarring and thickening in the lungs with difficulties in breathing, sometimes fatal (interstitial lung disease),
- Reversible short-term loss of vision.

Very rare (affects less than 1 person in 10,000)

- Presence of blood or dark brown coffee-coloured particles in your vomit.

Frequency unknown (cannot be assessed)

- Convulsion.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

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.

Storing your medicine

Do not freeze the unopened vial. Keep the vial in the outer carton to protect from light.

Storage conditions for the reconstituted and diluted solutions are given in the information intended for medical or healthcare professionals.

Do not use this medicine if you notice any visible particles.

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. One ml of reconstituted solution for infusion contains 5 mg of oxaliplatin.
- 50 mg vial: each vial contains 50 mg of oxaliplatin for reconstitution in 10 ml of solvent.
- 100 mg vial: each vial contains 100 mg of oxaliplatin for reconstitution in 20 ml of solvent.

The other ingredient is lactose monohydrate.

What Oxaliplatin looks like and contents of the pack

Oxaliplatin is a white to grey white powder, which is provided in a glass vial with Lyotec rubber stopper and Aluminum flip-off tear-off seal with green (for 50 mg/vial) & blue (for 100 mg/vial), polypropylene flip cap containing 50 mg or 100 mg of Oxaliplatin. The vials are supplied in cartons of one vial.

Not all pack sizes may be marketed.

Marketing authorisation holder and manufacturer

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

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

Belgium	Oxaliplatine Fresenius Kabi 5 mg/ml poeder voor oplossing voor infusie
Czech republic	Oxaliplatin Kabi 5 mg/ml prášek pro připravu infuzniho roztoku
Germany	Oxaliplatin Kabi 5 mg/ml Pulver zur Herstellung einer Infusionslösung
Estonia	Oxaliplatin Kabi 5 mg/ml
Finland	Oxaliplatin Fresenius Kabi 5 mg/ml
Hungary	Oxaliplatin Fresenius Kabi 5 mg/ml por oldatos infúzióhoz
Ireland	Oxaliplatin 5 mg/ml powder for solution for infusion
Italy	Oxaliplatino Kabi 5 mg/ml polvere per soluzione per infusione
Latvia	Oxaliplatin Kabi 5 mg/ml pulveris infūziju šķīduma pagatavošanai
Lithuania	Oxaliplatin Kabi 5 mg/ml milteliai infuziniam tirpalui
Norway	Oxaliplatin Fresenius Kabi 5 mg/ml pulver til infusjonsvæske, oppløsning
Poland	Oxaliplatin Kabi
Portugal	Oxaliplatina Kabi
Romania	Oxaliplatin Kabi 5 mg/ml pulbere pentru soluție perfuzabilă
Spain	Oxaliplatino Kabi 5 mg/ml polvo para solución para perfusión
Slovak Republic	Oxaliplatin Kabi 5 mg/ml prášok na infúzny roztok
Sweden	Oxaliplatin Fresenius Kabi 5 mg/ml pulver till infusionsvätska, lösning

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used to reconstitute the solution.

- For a 50 mg vial: add 10 ml solvent to obtain a solution of 5 mg oxaliplatin per ml.
- For a 100 mg vial: add 20 ml solvent to obtain a solution of 5 mg oxaliplatin per ml.

Inspect the reconstituted solution visually prior to use. Only clear solutions without particles should be used.

The reconstituted solution can be stored for 24 hours in the refrigerator (2°C-8°C).

The vial should reach room temperature before being pierced.

The medicinal product is for single use only. Any unused solution should be discarded.

Dilution for intravenous infusion

Withdraw the required amount of concentrate from the vial(s) and then dilute with 250 ml to 500 ml of a glucose 5% (50 mg/ml) solution to obtain an oxaliplatin concentration between 0.20 mg/ml and 0.60 mg/ml. The concentration range over which the physico-chemical stability of oxaliplatin has been demonstrated is 0.20 mg/ml to 0.60 mg/ml.

Administer by intravenous infusion.

After dilution in glucose 5% (50 mg/ml) solution, chemical and physical in-use stability has been demonstrated for 24 hours at 2°C -8°C and for 6 hours at 20°C -25°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 the solution 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 (see chapter "disposal" below).

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 ml to 500 ml of a glucose 5% (50 mg/ml) 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. 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 of in accordance with local requirements.

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