Kalcex

Package leaflet: Information for the user

Oxaliplatin 5 mg/ml concentrate for solution for infusion

oxaliplatin

Read all of this leaflet carefully before you are given 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 nurse.
- If you get any side effects, talk to your doctor 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

The active ingredient of this medicine is oxaliplatin.

Oxaliplatin is used to treat cancer of the large bowel in adults (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 (5-FU) and folinic acid (FA).

Oxaliplatin is an anticancer drug and contains platinum.

2. What you need to know before you are given Oxaliplatin

You should not be given Oxaliplatin if:
- you are allergic to oxaliplatin or to any of the other ingredients of this medicine (listed in section 6)
- you are breast-feeding
- you already have a reduced number of blood cells
- you already have tingling and numbness in the fingers and/or toes, and have difficulty performing delicate tasks, such as buttoning clothes
- you have severe kidney problems.

Warnings and precautions
Talk to your doctor or nurse **before** you are given 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.
- you have mild or moderate kidney problems
- you have any liver problems or abnormal liver function test results during your treatment
- you have or had heart disorders such as an abnormal electrical signal called prolongation of the QT interval, an irregular heartbeat, or a family history of heart problems
- you have recently received or plan to receive any vaccines. During treatment with oxaliplatin, you should not have a vaccination with "live" or "attenuated" vaccines, such as yellow fever vaccine.

Children and adolescents
Oxaliplatin should not be used in children and adolescents below 18 years of age.

Other medicines and Oxaliplatin
Tell your doctor if you are using, have recently used or might use 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 for advice before you are given this medicine.

- 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 9 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.

Fertility
- Oxaliplatin may have an anti-fertility effect, which could be irreversible. Male patients should seek advice on conservation of sperm prior to treatment.
- Male patients are advised not to father a child during treatment and 6 months after treatment, and to take appropriate contraceptive measures during this time.

Driving and using machines
Oxaliplatin treatment may result in an increased risk of dizziness, nausea and vomiting, and other neurologic symptoms that affect walking and balance. If this happens, you should not drive or operate machinery. If you have vision problems during treatment with oxaliplatin, do not drive, operate machines, or engage in dangerous activities.

3. How Oxaliplatin is given

For intravenous infusion.
Oxaliplatin is intended only for adults.
Oxaliplatin concentrate for solution for infusion is administered by medical personnel and has to be dissolved and made into a solution before it can be injected into a vein.

Dose
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/m^2 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 will be given by slow intravenous infusion (drip) into one of your veins 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 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 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 (due to a reduction in platelets or a reduction in white blood cells),
- 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,
- 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),
- Stroke symptoms (including sudden severe headache, confusion, trouble seeing in one or both eyes, numbness or weakness of face, arm or leg usually on one side, face drooping, trouble walking, dizziness, loss of balance and speech difficulty),
- Extreme tiredness with decreased number of red blood cells, and shortness of breath (haemolytic anaemia), alone or combined with low platelet count and kidney disease where you pass little or no urine (symptoms of haemolytic-uraemic syndrome), which may be fatal.

Other known side effects of oxaliplatin are:

Very common (may affect more than 1 in 10 people)
- Oxaliplatin 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

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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 preparation of injectable solutions of cytotoxic agents must be carried out by trained and specialized personnel with knowledge of the medicines used, in conditions that guarantee the integrity of the 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 subsection “Disposal” below).

If oxaliplatin concentrate or solution for infusion comes into contact with the skin, the skin should be washed immediately and thoroughly with water.

If oxaliplatin concentrate or infusion solution comes into contact with mucous membranes, wash the mucous membranes immediately and thoroughly with water.

Special precautions for administration

- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only 50 mg/ml (5 %) glucose 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 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 other drugs. Alkaline drugs or solutions will adversely affect the stability of oxaliplatin.

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

Oxaliplatin 85 mg/m^2 intravenous infusion in 250 to 500 ml of 50 mg/ml (5 %) glucose solution is given at the same time as folinic acid intravenous infusion in 50 mg/ml (5 %) glucose 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 50 mg/ml (5 %) glucose solution, never in alkaline solutions or sodium chloride or chloride containing solutions.

Instruction for use with 5-fluorouracil (5-FU)

Oxaliplatin should always be administered before fluoropyrimidines – i.e. 5-fluorouracil.

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

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

Concentrate for solution for infusion

Inspect the medicinal product visually prior to use. Only clear solutions without particles should be used.

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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 (may affect up to 1 in 10 people)
- Infection due to a reduction in white blood cells,
- Serious infection of the blood in addition to a reduction in white blood cells (neutropenic sepsis), which may be fatal,
- Reduction in white blood cells accompanied by temperature > 38.3 °C or a prolonged temperature > 38 °C for more than one hour (febrile neutropenia),
- Presence of blood or dark brown coffee-coloured particles in your vomit,
- Indigestion and heartburn, hiccups, flushing, dizziness,
- Increased sweating and nail disorders, flaking skin,
- Chest pain,
- 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,
- Decreased levels of calcium in the blood,
- Fall.

Uncommon (may affect up to 1 in 100 people)
- Serious infection of the blood (sepsis), which may be fatal,
- Decreased blood pH (metabolic acidosis),
- Difficulty in hearing, vertigo, ringing in ears,
- Blockage or swelling of the bowel,
- Nervousness.

Rare (may affect up to 1 in 1 000 people)
- Loss of hearing,
- Scarring and thickening in the lungs with difficulties in breathing, sometimes fatal (interstitial lung disease),
- Reversible short-term loss of vision,
- Unexpected bleeding or bruising due to widespread blood clots throughout the small blood vessels of the body (disseminated intravascular coagulation), which may be fatal.

Very rare (may affect up to 1 in 10 000 people)
- Kidney disease where you pass little or no urine (symptoms of acute renal failure),
- Vascular disorders of the liver.

Not known (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), pancytopenia,
- Serious infection of the blood and low blood pressure (septic shock), which may be fatal,
- Convulsion (uncontrolled shaking of the body),
- Spasm of the throat causing difficulty in breathing,
- Pneumonia (serious lung infection), which may be fatal,
- Extreme tiredness with decreased number of red blood cells, and shortness of breath (haemolytic anaemia), alone or combined with low platelet count and kidney disease where you pass little or no urine (symptoms of haemolytic-uraemic syndrome), which may be fatal, have been reported,
- Abnormal heart rhythm (QT prolongation), that can be seen on electrocardiogram (ECG), which may be fatal,
- Heart attack (myocardial infarction), pain or uncomfortable feeling in the chest (angina pectoris),
- Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal,
- Inflammation of the lining of the oesophagus – the tube that connects your mouth with your stomach – resulting in pain and swallowing difficulty (oesophageal inflammation),
- Abdominal pain, nausea, bloody vomit or vomit that looks like “coffee grounds”, or dark coloured/tarry stools (symptoms of gastrointestinal ulcer, with potential bleeding or perforation), which may be fatal,
- Decreased blood flow to the intestine/bowel (intestinal ischaemia), which may be fatal,
- Risk of new cancers. Leukaemia, a form of blood cancer, has been reported in patients after taking oxaliplatin in combination with certain other medicines. Talk to your doctor about the potential for increased risk of this type of cancer when taking oxaliplatin and certain other medicines,
- Non-cancerous abnormal liver nodules (focal nodular hyperplasia).

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 via Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

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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.

This medicinal product does not require any special storage conditions.

Shelf life after dilution
Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C and 4 days at 2 to 8 °C when diluted with glucose 50 mg/ml (5 %) solution in concentrations between 0.2 mg/ml and 2 mg/ml.

From a microbiological point of view, the diluted product 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 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Oxaliplatin must not come into contact with the eyes or the skin. If such an incident occurs, inform your doctor or nurse **immediately**.

As soon as the infusion is finished, the unused medicine must be carefully discarded by the doctor or the nurse.

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.
Each ml of concentrate for solution for infusion contains 5 mg oxaliplatin.
Each vial with 10 ml concentrate contains 50 mg oxaliplatin.
Each vial with 20 ml concentrate contains 100 mg oxaliplatin.
Each vial with 40 ml concentrate contains 200 mg oxaliplatin.

− The other ingredient is water for injections.

What Oxaliplatin looks like and contents of the pack
This medicine is a concentrate for solution for infusion (sterile concentrate). It is a clear, colourless solution practically free from visible particles.

10 ml, 20 ml or 40 ml of solution in colourless glass vial, sealed with rubber stopper and aluminium flip-off seal. Vials are packed in outer cartons.

Pack sizes: 1 vial with 10 ml, 20 ml or 40 ml

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
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Place for AS Kalceks internal code

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 subsection “Disposal” below).
For single use only. Any unused concentrate should be discarded (see subsection “Disposal” below).

Dilution for intravenous infusion

USE ONLY the recommended solvent (only 50 mg/ml (5 %) glucose infusion solution).

Withdraw the required amount of concentrate solution from the vial(s) and then dilute with 250 ml to 500 ml of a 50 mg/ml (5 %) glucose solution to give an oxaliplatin concentration between 0.2 mg/ml and 0.7 mg/ml; concentration range for which the physico-chemical stability of oxaliplatin has been demonstrated is between 0.2 mg/ml and 2 mg/ml.

Administer by intravenous infusion.

Chemical and physical in use stability has been demonstrated for 24 hours at 25 °C and 4 days at 2 to 8 °C when diluted with glucose 50 mg/ml (5 %) solution in concentrations between 0.2 mg/ml and 2 mg/ml.

From a microbiological point of view, the diluted product 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 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

NEVER use sodium chloride or chloride containing solutions for dilution.

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

Inspect the diluted solution visually prior to use. Only clear solutions without particles should be used. Any unused solution should be discarded (see subsection “Disposal” below).

Infusion

The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 to 500 ml of a 50 mg/ml (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

Remnants of the medicinal product as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents and with due regard to current laws related to the disposal of hazardous waste.

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