PACKAGE LEAFLET: INFORMATION FOR THE USER

Oxaliplatin 5mg/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

Oxaliplatin is an anticancer medicine and contains the active substance oxaliplatin.

Oxaliplatin is used for treating bowel cancer after it has been removed by surgery or when it has already spread.

Oxaliplatin is used in combination with other anticancer medicines called 5- fluorouracil (5-FU) and folinic acid (FA).

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN OXALIPLATIN

You should not be given Oxaliplatin:
1. if you are **allergic** to oxaliplatin
2. if you are **breast-feeding**
3. if you already have a **reduced number of blood cells**
4. if you already have **tingling and numbness in the fingers and/or toes**, and have **difficulty performing delicate tasks**, such as buttoning clothes
5. if you have **severe kidney problems**

Warnings and precautions:
Talk to your doctor 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.
- if you have mild or moderate kidney problems.
- if you have any liver problems or abnormal liver function test results during your treatment.
- If you have or had heart disorders such as an abnormal electrical signal called prolongation of the QT interval, an irregular heart beat, or a family history of heart problems.

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
- 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.

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 until 6 months after treatment, and to take appropriate contraceptive measures during this time.

Ask your doctor or pharmacist for advice before taking any 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 OXALIPLATIN IS USED

This medicine will be administered by medical personnel; do not take it yourself. Oxaliplatin is intended in adults 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. If feelings of discomfort or pain arise at the injection site inform the healthcare professionals immediately.
- 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 received more Oxaliplatin than you should
As this medicine is administered by a healthcare professional it is highly unlikely that you will be given too much or too little.

In case of overdose you may experience increased side effects. Your doctor may give you appropriate treatment for these side effects.

If administration of Oxaliplatin is forgotten
Your doctor will decide on what time you will receive this medicine. If you think you missed a dose, please contact your doctor as soon as possible.

If you have any questions about your treatment ask your doctor or pharmacist.

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.

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 (very common).
- Abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature (very common).
- Persistent or severe diarrhoea or vomiting (very common).
- Respiratory symptoms such as dry or wet cough, difficulties in breathing or crackles (very common), shortness of breath and wheezing as these may be indicators of a serious lung disease that may lead to death.
- Stomatitis/mucositis (sore lips or mouth ulcers) (very common).
- Presence of blood or dark brown coffee-coloured particles in your vomit (common).
- 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) (rare).
- 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) (rare), alone or combined with low platelet count, abnormal bruising (thrombocytopenia) (rare) and kidney disease where you pass little or no urine (symptoms of Haemolytic-uraemic syndrome) (frequency not known).
- Tingling and/or numbness in the fingers, toes, around the mouth or in the throat that may sometimes occur in association with cramps and can also lead to difficulty in performing delicate tasks, such as buttoning clothes (symptoms of a peripheral neuropathy) (very common)

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 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 diarrhea, 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.
- 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 fever > 38.3°C or a prolonged fever > 38°C for more than one hour (febrile neutropenia).
- Indigestion and heartburn, flushing, hiccups and 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 of kidney function, change 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.
- 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 liver.

Frequency not known (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.
- 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.
- Myocardial infarction (Heart attack), anginapectoris (pain or uncomfortable feeling in the chest).
- Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal.
- Oesophageal inflammation (inflammation of the lining of the esophagus - the tube that connects your mouth with your stomach resulting in pain and swallowing difficulty).
- Abdominal pain, nausea, bloody vomit or vomit that looks like “coffee grounds”, or dark colored/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. Leukemia, 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.

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 specialist personnel with knowledge of the medicinal products 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 medicinal products, 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 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.

Special precautions for administration
- DO NOT use injection material 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 solution 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 medicinal products or solutions, in particular 5-fluorouracil, folinic acid products containing trometamol as an excipient and trometamol salts of other products. Alkaline medicinal products or solution will adversely affect the stability of oxaliplatin.

Instructions for use with folinic acid (as calcium folinate or disodium folinate)
Oxaliplatin 85mg/m² IV infusion in 250 to 500 ml of 5% glucose solution is given at the same time as folinic acid IV infusion in 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 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.
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 visually prior to use. Only clear solutions free from visible particles should be used. This medicinal product is for single use only. Any unused concentrate 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 5% glucose solution to give an oxaliplatin concentration not less than 0.25 mg/ml.

Administer by intravenous infusion.

From a microbiological point of view, the 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 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 to 8°C when diluted to the concentrations of 0.25 mg/ml with glucose 5% as well as for 6 hours at 20-25°C when diluted to the concentration of 0.25 mg/ml with glucose 5%.

Inspect visually prior to use. Only clear solutions free from visible 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 solution for dilution.

Infusion
The administration of oxaliplatin does not require prehydration.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the 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.

5. HOW TO STORE OXALIPLATIN

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

Oxaliplatin should not come into contact with the eyes or skin. If there is any accidental spillage, tell the doctor or nurse immediately.

Prior to mixing this medicinal product must be kept in the outer carton in order to be protected from light and must not be frozen.
Do not store above 25°C.

In-use stability after dilution
From a microbiological point of view, the 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.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 to 8 °C when diluted to the concentrations of 0.25 mg/ml and with glucose 5% as well as for 6 hours at 20-25 °C when diluted to the concentration of 0.25 mg/ml with glucose 5%.

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

When the infusion has finished, Oxaliplatin will be disposed of carefully by the doctor or nurse.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Oxaliplatin contains
- The active substance is oxaliplatin.
- The other ingredient is water for injections

What Oxaliplatin looks like and contents of the pack
Clear, colourless solution. It is free from visible particles.

1 ml of solution contains 5 mg oxaliplatin as active ingredient.

This medicinal product is a concentrate for solution for infusion.

10 ml of concentrate for solution for infusion contain 50 mg of oxaliplatin.
20 ml of concentrate for solution for infusion contain 100 mg of oxaliplatin.
40 ml of concentrate for solution for infusion contain 200 mg of oxaliplatin.

Pack sizes:
50mg/10ml: 1 vial
100mg/20ml: 1 vial
200mg/40ml: 1 vial

With or without a protective plastic overwrap.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Hikma Farmacêutica (Portugal), S.A.
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Distributed by
Consilient Health (UK) Ltd.,
No.1 Church Road, Richmond upon Thames,
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This leaflet was last revised in July 2021.

Consilient Health

P1347

Oxaliplatin diluted in 250 to 500 ml of a 5% glucose solution to give a concentration not less than 0.25 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 in accordance with local requirements related to the disposal of hazardous waste.

Administration
FOR ADULTS ONLY

The recommended dose for oxaliplatin in adjuvant setting is 85 mg/m² intravenously repeated every two weeks for 12 cycles (6 months).

The recommended dose for oxaliplatin in treatment of metastatic colorectal cancer is 85 mg/m² intravenously repeated every 2 weeks until disease progression or unacceptable toxicity.

Dosage given should be adjusted according to tolerability (see 4.4 “Special warnings and precautions for use” in the corresponding SPC).

Oxaliplatin **should always** be administered before **fluoropyrimidines -i.e. 5-fluorouracil**. Oxaliplatin is administered as a 2-to-6-hour intravenous infusion in 250 to 500 ml of 5% glucose solution (50mg/ml) to give a concentration between 0.2 mg/ml and 0.70 mg/ml; 0.7 mg/ml is the highest concentration in clinical practice for an oxaliplatin dose of 85 mg/m^2.

Shelf life
Medicinal product as packaged for sale: 24 months

In-use stability after dilution
From a microbiological point of view, the 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 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 to 8 °C when diluted to the concentrations of 0.25 mg/ml with glucose 5% as well as for 6 hours at 20-25 °C when diluted to the concentration of 0.25 mg/ml with glucose 5%.

Special precautions for storage
Keep the vial in the outer carton in order to protect from light. Do not freeze.
Do not store above 25°C.