

PACKAGE LEAFLET

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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. 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

Oxaliplatin is an anticancer drug that contains platinum.

Oxaliplatin 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 anticancer agents, 5-fluorouracil and folinic acid.

2. What you need to know before you use Oxaliplatin

You should not be given Oxaliplatin if

- you are allergic to oxaliplatin or 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 (white blood cells and/or platelets)
- 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.

Even if you are male, please ensure that you read the section of this leaflet that concerns pregnancy and breast-feeding.

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 or cisplatin
- you have moderate kidney problems
- 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 heartbeat, or a family history of heart problems
- if 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.

If any of the following applies to you at any time, tell your doctor immediately. Your doctor may need to treat you for these events. Your doctor may need to reduce the dose of Oxaliplatin, or delay or stop your treatment with Oxaliplatin.

- If you have an unpleasant sensation in the throat, in particular when swallowing, and have a sensation of shortness of breath, during the treatment, tell your doctor.
- If you have nerve problems in your hands or feet, such as numbness or tingling, or decreased sensations in your hands or feet, tell your doctor.
- If you have headache, altered mental functioning, seizures and abnormal vision from blurriness to vision loss, tell your doctor.
- If you feel or are sick (nausea or vomiting), tell your doctor.
- If you have severe diarrhoea, tell your doctor.
- If you have sore lips or mouth ulcers (mucositis/ stomatitis), tell your doctor.
- If you have diarrhoea, or a reduction in white blood cells or platelets, tell your doctor. Your doctor may reduce the dose of Oxaliplatin or postpone your treatment with Oxaliplatin.
- If you have unexplained respiratory symptoms such as cough, or any difficulties in breathing, tell your doctor. Your doctor may stop your treatment with Oxaliplatin.
- If you develop an extreme tiredness, shortness of breath, or kidney disease where you pass little or no urine (symptoms of acute renal failure), tell your doctor.
- If you have fever (temperature greater than or equal to 38°C), or chills, which could be signs of infection, tell your doctor immediately. You may be at risk of getting an infection of the blood.
- If you have fever > 38°C, tell your doctor. Your doctor may determine you also have a reduction in white blood cells.
- If you experience unexpected bleeding or bruising (disseminated intravascular coagulation), tell your doctor as these could be signs of blood clots throughout the small vessels of your body.
- If you faint (lose consciousness) or have an irregular heartbeat while being given Oxaliplatin, tell your doctor immediately as this may be a sign of a serious heart condition.
- If you experience muscle pain and swelling, in combination with weakness, fever, or red-brown urine, tell your doctor. These could be signs of muscle damage (rhabdomyolysis) and could lead to kidney problems or other complications.
- If you have abdominal pain, nausea, bloody vomit or vomit that looks like “coffee-grounds”, or dark-coloured/ tarry stools, which may be signs of an ulcer of the bowel (gastrointestinal ulcer, with potential bleeding or perforation), tell your doctor.
- If you have abdominal (tummy) pain, bloody diarrhoea, and nausea and/or vomiting, which may be caused by a reduction of blood flow to your gut wall (intestinal ischaemia), tell your doctor.

Children

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

Other medicines and Oxaliplatin

Tell your doctor or pharmacist 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 increased 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 being given oxaliplatin, do not drive, operate heavy machines, or engage in dangerous activities.

3. How to use Oxaliplatin

Oxaliplatin may only be given to adults.
For single use only.

Dosage

The dose of Oxaliplatin is based on your body surface area (calculated from your height and weight). The dose will also depend on results of blood tests and whether you have previously experienced side effects with Oxaliplatin.

The recommended dose for adults including the elderly is 85 mg/m² of body surface.

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.
- 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 nurse or doctor immediately.

Frequency of administration

You should usually receive your infusion once every two 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 use 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 you have any further questions on the use of this medicine, ask your doctor.

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.

Most serious side effects

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

Very common: *may affect more than 1 in 10 people*

- allergies/allergic reactions, occurring mainly during infusion, sometimes fatal
- stomatitis / mucositis (sore lips or mouth ulcers)
- low platelet count, abnormal bruising (thrombocytopenia). Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course.
- unexplained respiratory symptoms such as dry cough, difficulties in breathing or crackles.

Common: *may affect up to 1 in 10 people*

- 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 $> 38.3^{\circ}\text{C}$ or a prolonged fever $> 38^{\circ}\text{C}$ for more than one hour (febrile neutropenia)
- 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.
- pain in the chest or upper back, difficulty breathing and coughing up blood (symptoms of clots in the lungs).

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
- difficulty in hearing, vertigo, ringing in ears.

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

- unexpected bleeding or bruising due to widespread blood clots throughout the small blood vessels of the body (disseminated intravascular coagulation), which may be fatal
- abnormal bruising, bleeding or signs of infection such as a sore throat and high temperature
- persistent or severe diarrhoea or vomiting
- reversible short-term loss of vision
- 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)
- extreme tiredness with decreased number of red blood cells, and shortness of breath (haemolytic anaemia), alone or combined with low platelet count, abnormal bruising (thrombocytopenia) and kidney disease where you pass little or no urine (symptoms of Haemolytic-uraemic syndrome)
- scarring and thickening in the lungs with difficulties in breathing, sometimes fatal (interstitial lung disease)
- pain in upper abdomen and pain associated with nausea and vomiting.

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 (symptoms include abdominal pain and swelling, weight gain and tissue swelling of the feet, ankles or other parts of the body).

Not known: *frequency cannot be estimated from the available data*

- serious infection of the blood and low blood pressure (septic shock), which may be fatal

- abnormal heart rhythm (QT prolongation), that can be seen on electrocardiogram (ECG), which may be fatal
- muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal
- 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
- spasm of the throat causing difficulty in breathing
- auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia) (symptoms include easy bleeding, easy bruising, shortness of breath, extreme lethargy and weakness, and an increased risk of infection due to the immune compromised state)
- 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)
- pneumonia (serious lung infection) which may be fatal
- Non-cancerous abnormal liver nodules (focal nodular hyperplasia).

Other known side effects

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 disappear 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 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
- abnormal tongue sensation possibly altering speech
- stomach pain
- abnormal bleeding including nose bleeds
- allergic reactions, skin rash including red and itchy skin, mild hair loss (alopecia)
- alteration in blood tests including those relating to abnormalities on liver function.

Common: may affect up to 1 in 10 people

- indigestion and heart burn, hiccups, flushing 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 in kidney function, changes of frequency of urination, dehydration
- blood in the urine/stools, swelling of the veins
- high blood pressure
- depression and sleeplessness (insomnia)
- conjunctivitis and visual problems
- decreased levels of calcium in the blood
- swelling of the nerves to the muscles, neck stiffness
- fall.

Uncommon: may affect up to 1 in 100 people

- nervousness.

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

- loss of hearing.

Not known: frequency cannot be estimated from the available data

- allergic vasculitis (inflammation of blood vessels)
- convulsion (uncontrolled shaking of the body)
- myocardial infarction (heart attack), angina pectoris (pain or uncomfortable feeling in the chest)
- oesophageal inflammation (inflammation of the lining of the oesophagus - the tube that connects your mouth with your stomach- resulting in pain and swallowing difficulty)
- risk of new cancers. Leukemia, a form of blood cancer, has been reported in patients after taking oxaliplatin concentrate for solution for infusion in combination with certain other medicines. Talk to your doctor about the potential for increased risk of this type of cancer when you are given Oxaliplatin 5 mg/ml concentrate for solution for infusion and certain other medicines.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: 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.
Do not store above 25°C.

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.

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 5 mg/ml concentrate for solution for infusion contains

- The active substance is oxaliplatin.

- One ml of concentrate contains 5 mg oxaliplatin.
- A vial of 10 ml of concentrate contains 50 mg oxaliplatin.
- A vial of 20 ml of concentrate contains 100 mg oxaliplatin.
- A vial of 40 ml of concentrate contains 200 mg oxaliplatin.
- The other ingredients are lactose monohydrate and water for injection.

What Oxaliplatin 5 mg/ml concentrate for solution for infusion looks like and contents of the pack

Concentrate for solution for infusion: clear colourless solution in a vial. It is available in 10 ml, 20 ml and 40 ml vials in boxes of 1 or 5 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Sun Pharmaceutical Industries Europe B.V.
Polarisavenue 87
2132 JH Hoofddorp
The Netherlands

This medicine is authorised in the Member states of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Germany	Oxaliplatin SUN 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
France	Oxaliplatine SUN 5 mg/ml solution à diluer pour perfusion
Italy	Oxaliplatino SUN 5 mg/ml concentrato per soluzione per infusione
Spain	Oxaliplatino SUN 5 mg/ml concentrado para solución para perfusión EFG
The Netherlands	Oxaliplatine SUN 5 mg/ml concentraat voor oplossing voor infusie
Norway	Oksaliplatin SUN 5 mg/ml konsentrat til infusjonsvæske, oppløsning
United Kingdom (Northern Ireland)	Oxaliplatin 5 mg/ml concentrate for solution for infusion

This leaflet was last revised in November 2023.

The following information is intended for medical or healthcare professionals only:

Oxaliplatin 5 mg/ml, concentrate for solution for infusion

Instructions for handling and disposal

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

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 suitable labelled rigid containers. See below under “*Disposal*”.

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

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

Disposal

Remnants of the medicinal product as well as all materials that have been used for dilution and administration must be destroyed according to standard procedures applicable to cytotoxic agents in accordance with local requirements related to the disposal of hazardous waste.

Special precautions for administration

DO NOT use injection equipment containing aluminium.

DO NOT administer oxaliplatin undiluted.

Only glucose 5% (50 mg/ml) solution for infusion 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 medicinal products or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of others 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 glucose 5% (50 mg/ml) solution is given at the same time as folinic acid intravenous infusion in glucose 5% 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% solution, never in alkaline solutions or sodium 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 medicinal products combined with oxaliplatin, see the corresponding summary of product characteristics.

Incompatibilities

This medicinal product should not be mixed with other medicinal products except for those mentioned in the section “Instructions for dilution”.

Instructions for dilution

Only 5% glucose solution should be used to dilute the concentrate.

Withdraw the required amount of concentrate from the vial(s) and then dilute with 250 to 500 ml of a 5% glucose solution to give an oxaliplatin concentration between not less than 0.2 mg/ml and 0.7 mg/ml, i.e. the concentration range over which the physico-chemical stability for oxaliplatin has been demonstrated.

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

Infusion

The administration of oxaliplatin does not require prehydration.
Oxaliplatin diluted in 250 to 500 ml of a 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.

Storage conditions

Medicinal product as packaged for sale:
Do not store above 25°C.

Infusion preparation:

After dilution with 5% glucose solution, chemical and physical in-use stability has been demonstrated for 24 hours at room temperature (15°C-25°C) or for 48 hours under refrigeration (2°C-8°C). From a microbiological point of view, the 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.