

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

1 What Oxaliplatin 5 mg/ml is and what it is used for

Oxaliplatin 5 mg/ml is a cytostatic (anticancer medicine) and is used to treat metastatic (advanced) cancer of the large bowel (colon and rectum) or as additional treatment following surgery to remove a tumor (growth) in the colon. Oxaliplatin is used in combination with other anticancer medicines, called 5-fluorouracil (5-FU) and leucovorin (folinic acid).

2 What you need to know before Oxaliplatin 5 mg/ml is administered to you

Do not use Oxaliplatin 5 mg/ml:

(see also section “Warnings and precautions”)

- if you are **allergic** to oxaliplatin, or any of the other ingredients of this medicine (listed in section 6)
- if you are **breast-feeding** (see also section ‘Pregnancy, breast-feeding and fertility’)
- 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 in performing delicate tasks, such as buttoning clothes
- if you have **severe kidney problems**.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you receive Oxaliplatin 5 mg/ml if you

- experience abnormal feeling of **pain or tingling** in the fingers, feet, around the mouth or throat, during or several hours after treatment. This can also happen after exposure to cold (for instance after drinking cold drinks).
- have **moderate kidney problems**.
- have **any liver problems**.
- ever have suffered an **allergic** reaction to platinum-containing medicines, such as carboplatin or cisplatin.
- experience **inflammation of the mucosa** (of the mouth).
- experience **unexplainable breathing problems**. Oxaliplatin 5 mg/ml administration will be stopped until a lung disorder can be excluded.

You will regularly have **neurological examinations** (see also section 4 “Possible side effects”).

This therapy can cause a decrease of blood cells. Therefore, your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course. This is necessary to continue therapy (see also section 2 “Do not use Oxaliplatin 5 mg/ml”).

Your doctor may prescribe antisickness medicines to prevent nausea (feeling sick) and vomiting (being sick).

Other medicines and Oxaliplatin 5 mg/ml

Tell your doctor or pharmacist if you are taking/using, have recently taken/used or might take/use any other medicines, including medicines obtained without prescription.

Pregnancy, breast-feeding and fertility

This medicine *should not be used during pregnancy*, because animal studies have shown a possible risk of abnormalities in the developing foetus.

Women should use *contraceptive measures* during and up to 4 months after therapy. 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.

This medicine must not be used during *breast-feeding*.

Oxaliplatin may have an *anti-fertility effect*, which could be permanent. Male patients are therefore advised not to father a child and to use *contraceptive measures* during and up to 6 months after treatment and to seek advice on preservation of sperm prior to treatment.

Driving and using machines:

No studies on the effect on the ability to drive and using machines have been performed. Oxaliplatin 5 mg/ml however, can cause side effects such as dizziness, nausea (feeling sick) and vomiting (being sick) and other neurological symptoms that effect gait and balance. If this happens you should not drive or operate machinery. If you have vision problems while receiving Oxaliplatin 5 mg/ml, do not drive, operate heavy machines, or engage in dangerous activities.

3 How Oxaliplatin 5 mg/ml is administered

Oxaliplatin 5 mg/ml is only used in *adults*.

Oxaliplatin 5 mg/ml will be prescribed for you by a specialist in cancer treatment. Carefully follow the advice of your doctor when Oxaliplatin 5 mg/ml is administered to you.

The administered amount (the dose) is dependent on the body surface and will be established by your doctor. Technically, this is measured in square metres (m²), but is actually calculated from your height and weight.

General guidance

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

Oxaliplatin 5 mg/ml is given by intravenous infusion (injection into a vein) over a 2 to 6 hours period.

The duration of the treatment will be determined by your doctor.

If oxaliplatin accidentally leaks out of the vein into the surrounding tissues while administered, the administration will be stopped immediately and appropriate measures will be taken.

If you received more Oxaliplatin 5 mg/ml 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.

There is no specific antidote for oxaliplatin overdose. 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 questions about the treatment, ask your doctor, pharmacist or nurse.

If administration of Oxaliplatin 5 mg/ml 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 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.

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 (being sick),
- 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).

You should stop taking Oxaliplatin 5 mg/ml and see your doctor immediately if you experience symptoms of angioedema, such as

- swollen face, tongue or pharynx
- difficulty to swallow
- hives and difficulties to breathe.

The following side effects can occur:

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

- Bacterial or viral infection.
- Reduction in the number of red blood cells (anaemia: this may cause tiredness), reduction in the number of platelets associated with bruises and abnormal bleeding (thrombocytopenia), reduction in the number of white blood cells associated with increased infection risk (neutropenia, leukopenia or lymphopenia).
- Hypersensitivity to certain chemicals associated with symptoms such as watery eyes, runny nose, rash or tightness of the chest (allergy/allergic reactions).
- Lack of appetite (anorexia), changes in blood glucose level (this can be recognised by great thirst, dry mouth or a need to urinate more often), low potassium in blood (this can be recognised by muscle cramps, muscle weakness or fatigue), abnormal sodium blood level (this can be recognised by tiredness and confusion).
- A disorder of 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 (Lhermitte's sign).
- Oxaliplatin can sometimes cause an unpleasant sensation in the throat, in particular when swallowing, and give the sensation of shortness of breath (pharyngolaryngeal dysaesthesia). This sensation, if it happens, usually occurs during or within hours of the infusion and may be triggered by exposure to 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.
- Abnormal sensation, change in taste, headache.
- Shortness of breath (dyspnoea), coughing, nose bleeds.
- Diarrhoea, nausea (feeling sick), vomiting (being sick) (medication to prevent the sickness is usually given to you by your doctor before treatment and may be continued after treatment), abdominal pain, constipation, sore mouth/lips or mouth ulcers (stomatitis/mucositis).
- Skin disorder, hair loss.
- Back pain.
- Increase in liver enzymes, increase in alkaline phosphatase in the blood, increase in bilirubin in the blood, increase in lactate dehydrogenase in the blood, weight gain (when oxaliplatin is given after primary therapy (adjuvant therapy)).
- Fever, rigors (tremors), fatigue, body weakness (asthenia), pain, reactions close to or at the injection site (e.g. local pain, redness, swelling during the infusion, blood clot formation, sometimes death of skin cells (skin necrosis)).

Common (*may affect up to 1 in 10 people*)

- Inflammation of the mucous membranes of the nose with symptoms of a stuffed nose, sneezing and nasal discharge (rhinitis), infection of the respiratory tract, infection due to a reduction in white blood cells (neutropenic sepsis).
- A serious condition (with fever) caused by a decrease of white blood cells associated with an increased susceptibility for infections (febrile neutropenia).
- Rash, conjunctivitis, inflammation of the mucous membranes of the nose with symptoms of a stuffed nose, sneezing and nasal discharge (rhinitis), shock (strong blood pressure drop, paleness, restlessness, rapid heart rate, moist skin, decreased consciousness) caused by a sudden vascular dilation as a result of a severe hypersensitivity reaction to certain substances (anaphylactic shock), tightness of the chest caused by cramping of the respiratory tract muscles (bronchospasm), chest pain, sudden swelling of the skin and mucosa (e.g. throat or tongue) (angio-oedema) and low blood pressure.
- A deficiency of body fluid (dehydration).
- Depression, sleeplessness.
- Dizziness, inflammation of the nerves associated with muscle weakness, difficulty with specific movements and sometimes muscle cramps (motor neuritis), neck stiffness (meningism).
- Conjunctivitis, visual problems.
- Bleeding (haemorrhage), flushing, inflammation of veins associated with blood clot formation (deep vein thrombosis), high blood pressure (hypertension).
- Hiccups, chest pain, blood clots in the lungs which cause chest pain and breathlessness (pulmonary embolism).
- Disturbed digestion with symptoms such as a feeling of fullness in your stomach, stomach pain, burping, nausea (feeling sick), vomiting (being sick) and heartburn (dyspepsia), regurgitation of acid and/or heartburn (gastroesophageal reflux), bleeding in the gastrointestinal tract or bleeding of the rectum (end of the bowel) (gastrointestinal haemorrhage, rectal haemorrhage).
- Flaking skin (Hand & foot syndrome), redness of the skin (erythematous rash), rash, increased perspiration (hyperhidrosis), nail disorder.
- Joint pain (arthralgia), bone pain.

- Blood in urine (haematuria), difficulty or pain on passing urine, abnormal frequency of passing urine.
- Increased blood creatinine level, weight loss (when oxaliplatin is given as therapy when the cancer has spread elsewhere in the body (metastasis)).

Uncommon (*may affect up to 1 in 100 people*)

- Blood tests which show an increase in acidity (metabolic acidosis)
- Nervousness
- Hearing problems
- Blockage (ileus) or swelling of the bowel (intestinal obstruction)

Rare (*may affect up to 1 in 1,000 people*)

- Blood abnormality (reduction in the number of platelets) caused by an allergic reaction associated with bruises and abnormal bleeding (immunoallergic thrombocytopenia), reduction in the number of red blood cells (anaemia) caused by degradation of blood (haemolytic anaemia)
- Speech disorder, neurologic disorder with symptoms such as headache, altered mental functioning, seizures and abnormal vision from blurriness to vision loss (reversible posterior leukoencephalopathy syndrome)
- Transient decrease of visual acuity, abnormal visual field, decrease in eyesight caused by inflammation of the optical nerve (optical neuritis), reversible transient loss of vision
- Deafness
- Scarring of the lungs which causes shortness of breath (pulmonary fibrosis) difficulties in breathing and/or scarring of the lungs, sometimes fatal (interstitial lung disease)
- Inflammation of the bowel (colitis), sometimes with diarrhoea, inflammation of the pancreas (pancreatitis).

Very rare (*may affect up to 1 in 10,000 people*)

- Liver disease that your doctor will monitor for you
- Changes in kidney function.

Unknown (*frequency cannot be estimated from the available data*)

- An abnormal, involuntary contraction of the muscles (convulsion)
- Occasionally other symptoms have been observed, like jaw and muscle spasms, coordination and balance problems, throat or chest tightness
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via 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 5 mg/ml

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

Store below 25°C. Keep the vial in the outer carton in order to protect from light.

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

When the infusion has finished, any remaining Oxaliplatin 5 mg/ml will be disposed of carefully by the doctor or nurse.

Medicines should not be disposed in wastewater or household waste. Ask your pharmacist how to dispose of medicines when no longer required. These measures will help protect the environment.

6 Contents of the pack and other information

What Oxaliplatin 5 mg/ml contains

- The active substance is oxaliplatin; 1 ml of concentrate for solution for infusion contains 5 mg of oxaliplatin.
- The other ingredients are lactose monohydrate and water for injections.

What Oxaliplatin 5 mg/ml looks like and contents of the pack

Oxaliplatin 5 mg/ml is a clear, colourless to almost colourless solution in a colourless glass vial with bromobutyl rubber stopper, aluminium seal and polypropylene snap-cap.

4 ml of concentrate for solution for infusion contains 20 mg of 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 vials are supplied in cartons each containing one vial.

Not all pack sizes may be marketed.

Manufacturers

Pharmachemie B.V.
Swensweg 5
P.O. Box 552
2003 RN Haarlem,
The Netherlands

Teva Pharmaceutical Works Private Limited Company
Táncsics Mihály út 82
2100 Gödöllő,
Hungary

Marketing Authorisation Holder

Pharmachemie B.V.
Swensweg 5, PO Box 552, 2003 RN Haarlem,
The Netherlands

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

Belgium	Oxaliplatine TEVA 5 mg/ml concentraat voor oplossing voor infusie
Czech republic	Oxaliplatin - Teva 5 mg/ml
Denmark	Oxaliplatin Teva
Estonia	Oxaliplatin-Teva 5mg/ml
Finland	Oxaliplatin Teva 5 mg/ml, infuusiokonsentraatti, liuosta varten
France	Oxaliplatine TEVA 5 mg/ml, solution à diluer pour perfusion
Germany	Oxaliplatin-GRY® 5 mg / ml Konzentrat zur Herstellung einer Infusionslösung
Greece	Oxaliplatin Teva 5 mg/ml, πυκνό διάλυμα για παρασκευή διαλύματος προς έγχυση
Hungary	Oxaliplatin-Teva 5 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Oxaliplatin 5 mg/ml, concentrate for solution for infusion
Italy	OxALIPLATINO TEVA 5 mg/ ml concentrato per soluzione per infusione
Latvia	Oxaliplatin-Teva 5mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania	Oxaliplatin-Teva 5 mg/ml koncentratas infuziniam tirpalui
Luxembourg	Oxaliplatine TEVA 5 mg/ml solution à diluer pour perfusion
Netherlands	Oxalisin 5 mg/ml, concentraat voor oplossing voor infusie
Norway	Oxaliplatin Teva 5 mg/ml, konsentrat til infusjonsvæske
Poland	Oxaliplatin Teva
Portugal	Oxaliplatina Teva 5mg/ml
Romania	Oxaliplatin Teva 5 mg/ml, concentrat pentru soluție perfuzabilă
Slovenia	Oksaliplatin Teva 5 mg/ml koncentrat za raztopino za infundiranje

Spain	Oxaliplatino TEVA 5mg/ml concentrado para solución para perfusión EFG
Sweden	Oxaliplatin Teva 5 mg/ml, koncentrat till infusionsvätska, lösning
United Kingdom	Oxaliplatin 5 mg/ml, concentrate for solution for infusion

This leaflet was last revised in 04/2016.

The following information is intended for medicinal and healthcare professionals only

PREPARATION GUIDE FOR USE WITH OXALIPLATIN 5 mg/ml CONCENTRATION FOR SOLUTION FOR INFUSION

It is important that you read the entire contents of this procedure prior to the preparation of Oxaliplatin 5 mg/ml, concentrate for solution for infusion.

1. Formulation

Oxaliplatin 5 mg/ml concentrate for solution for infusion is a clear, colourless or almost colourless liquid, containing 5 mg/ml oxaliplatin and 45 mg/ml lactose monohydrate in water for injections.

2. Presentation

Oxaliplatin 5 mg/ml is supplied as single-dose vials.

Oxaliplatin 5 mg/ml is a clear, colourless to almost colourless solution in a colourless glass vial with bromobutyl rubber stopper, aluminium seal and snap-cap.

4 ml of concentrate for solution for infusion contains 20 mg of 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.

Each box contains one Oxaliplatin 5 mg/ml vial.

Not all pack sizes may be marketed.

Oxaliplatin 5 mg/ml as packaged for sale:

Store below 25°C. Keep the vial in the outer carton in order to protect from light.

Solution for infusion:

After dilution in 5% glucose, chemical and physical in-use stability has been demonstrated for 24 hours at 2-8°C and for 6 hours at 25°C.

From a microbiological point of view, the infusion preparation should be used immediately.

If not used immediately, the 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.

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

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

3. Recommendations for safe 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 nursing or medical 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 protection of the environment and in particular the protection of the personnel handling the medicines. 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 for solution for infusion or infusion solution should come into contact with skin, wash immediately and thoroughly with water.

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

4. Preparation for the intravenous administration

Special precautions for administration

- DO NOT use injection material containing aluminium.
- DO NOT administer undiluted.
- ONLY dilute with 5% glucose solution. DO NOT dilute for infusion with saline or chloride containing solutions.
- DO NOT mix with any other medicinal product 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 (5-FU), folinic acid (FA) preparations containing trometamol as an excipient and trometamol salts of other active substances. The alkaline medicinal products or solutions will adversely affect the stability of oxaliplatin.

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

Oxaliplatin 85 mg/m² IV in 250 to 500 ml of 5% glucose solution can be co-administered with folinic acid (FA) IV infusion in 5% glucose solution during 2 to 6 hours, using a Y-line, which is placed immediately before the site of injection. These two medicinal products should not be combined in the same infusion bag. Folinic acid (FA) must not contain trometamol as an excipient and must only be diluted using isotonic infusion solutions such as 5% glucose solution but NOT sodium chloride solutions, chloride containing solutions or alkaline solutions.

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

Oxaliplatin should always be administered before fluoropyrimidines (eg. 5-fluorouracil (5-FU)). Always flush the line following oxaliplatin administration and only after that can 5-fluorouracil (5-FU) be administered.

4.1 Preparation of the infusion solution

Withdraw the required amount of solution 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, chemical and physical in-use stability has been demonstrated for 24 hours at 2-8°C and for 6 hours at 25°C.

From a microbiological point of view, this infusion prepared 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.

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

The medicinal product is for single use only. Any unused 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.

4.2 Infusion of the solution

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 (5-FU), the oxaliplatin infusion should precede that of 5-fluorouracil (5-FU).

4.3 Disposal

Remnants of the medicinal products 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.