Package leaflet: Information for the user

Oxaliplatin Eugia 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 pharmacist or nurse.
- 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 or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What <Invented Name> is and what it is used for

<Invented Name> contains active ingredient oxaliplatin which belong to a group of medicines based on platinum, which are used to treat cancer.

<Invented Name> is used to treat advanced cancer of the large bowel (especially after complete resection of primary tumour, metastatic cancer (cancer cells that spreads to other parts of the body) of colon and rectum). <Invented Name> is used in combination with other anticancer medicines called 5-fluorouracil and folinic acid.

2. What you need to know before you take <Invented Name>

Do not use <Invented Name> if:

- you are allergic to oxaliplatin.
- 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 pharmacist before using <Invented Name>:
- 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 moderate or mild kidney problems.
- If you have low blood values after previous treatment with oxaliplatin. Your doctor will have to perform tests to investigate if you have sufficient blood values before treatment starts;

- If you have symptoms of nerve injuries such as weakness, feeling of numbness, disturbance of taste or abnormal sensations after previous treatment with oxaliplatin. These symptoms can be caused by cold. Tell your doctor if you notice any of the symptoms, particularly if they are uncomfortable and/or last more than 7 days. Your doctor will perform neurological examinations, before and during treatment, particularly if you receive other medicines that can cause nerve injuries. Symptoms of nerve injuries may persist after end of treatment;
- If you also receive 5-fluorouracil, because of the increased risk of diarrhoea, vomiting, mouth ulcers and abnormal blood parameters.
- If you have liver problems
- 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 you are pregnant or planning a pregnancy (see Pregnancy, breast-feeding and fertility).
- Read the section about fertility even if you are a man.

Other medicines and <Invented Name>
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility
Pregnancy
- It is not recommended that you become pregnant during treatment with oxaliplatin and must use an effective method of contraception. Female patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 4 months.
- If you are pregnant or planning a pregnancy it is very important that you discuss this with your doctor **before** you receive any treatment.
- If you get pregnant during your treatment, you must immediately inform your doctor.

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

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 taking <Invented Name>, do not drive, operate heavy machines, or engage in dangerous activities.

3. How to take <Invented Name>

<Invented Name> is intended only for adults.

Dose
The dose of <Invented Name> 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 <Invented Name>.

Method and route of administration

- <Invented Name> 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 <Invented Name>.
- <Invented Name> is given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period.
- <Invented Name> will be given to you at the same time as folinic acid and before the infusion of 5-fluorouracil.

Frequency of administration
You should usually receive your infusion once every 2 weeks.

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

Your treatment will last a maximum of 6 months when used after complete resection of your tumour.

If you are given more <Invented Name> 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 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.

Seek immediate medical care you notice any of the following:
- Symptoms of an allergic 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 (may affect more than 1 in 10 people)
- Abnormal bruising or bleeding. Very common (may affect more than 1 in 10 people)
- Signs of infection such as a sore throat and high temperature. Common (may affect up to 1 in 10 people)
- Persistent or severe diarrhoea or vomiting. Very common (may affect more than 1 in 10 people)
- Presence of blood or dark brown coffee-coloured particles in your vomit. Very rare (may affect up to 1 in 10, 000)
- Sore lips or mouth ulcers. Very common (may affect more than 1 in 10 people)

- Unexplained respiratory symptoms such as dry or wet cough, difficulties in breathing or crackles, shortness of breath and wheezing. Very common (may affect more than 1 in 10 people)
- 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 (may affect up to 1 in 1,000 people)
- 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). Frequency not known (frequency cannot be estimated from the available data)

Other known side effects of <Invented Name> are:
Very common (may affect more than 1 in 10 people)
- <Invented Name> 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.
- <Invented Name> 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.
- <Invented Name> 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.
- <Invented Name> 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,
- 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,
- 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)
- Indigestion and heart burn, hiccups, flushing, dizziness,
- Increased sweating and nail disorders, flaking skin,
- Chest pain,
- 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,

- Red eyes and visual problems,
- Decreased levels of calcium in the blood.
- Fall

Uncommon (may affect up to 1 in 100 people)
- 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,

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

Frequency not known (frequency cannot be estimated from the available data)
- Allergic vasculitis (inflammation of blood vessels),
- Convulsion (uncontrolled shaking of the body),
- Spasm of the throat causing difficulty in breathing,
- Abnormal heart rhythm (QT prolongation), that can be seen on electrocardiogram (ECG), which may be fatal,
- Myocardial infarction (Heart attack), angina pectoris (pain or uncomfortable feeling in the chest).
- Oesophageal inflammation (inflammation of the lining of the esophagus - the tube that connects your mouth with your stomach- resulting in pain and swallowing difficulty).
- 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 <Invented Name> in combination with certain other medicines. Talk to your doctor about the potential for increased risk of this type of cancer when taking <Invented Name> 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V.* By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Invented Name>

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.

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

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

This medicinal product does not require any special storage conditions.

After dilution in 5% glucose, chemical and physical in-use stability has been demonstrated for 48 hours at 2°C to 8°C and for 24 hours at 25°C. From a microbiological point of view, the solution for infusion 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.

Do not use Oxaliplatin if you notice that the solution is not clear and free of particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What <Invented Name> contains

The active substances is oxaliplatin. Each vial contains 50 mg, 100 mg or 200 mg of oxaliplatin.
The other ingredient is water for injections.

What <Invented Name> looks like and contents of the pack

Concentrate for solution for infusion.

Clear, colourless solution, essentially free from visible particles. Each vial contains 50 mg, 100 mg or 200 mg oxaliplatin in water for injections. The vials are supplied in cartons of one vial.

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

Not all pack sizes may be marketed.

Marketing Authorisation Holder
[To be completed nationally]

Manufacturer
[To be completed nationally]

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

Belgium:	Oxaliplatin Eugia 5 mg/ml concentraat voor oplossing voor infusie / solution à diluer pour perfusion / Konzentrat zur Herstellung einer Infusionslösung
France:	OXALIPLATINE ARROW LAB 5mg/ml, solution à diluer pour perfusion
Germany:	Oxaliplatin PUREN 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Italy:	Oxaliplatino Aurobindo Italia
Poland:	Oxaliplatin Eugia
Portugal:	Oxaliplatina Generis
Spain:	Oxaliplatino Aurovit 5 mg/ml concentrado para solución para perfusión EFG
Sweden:	Oxaliplatin Eugia

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The following information is intended for medical or healthcare professionals only

PREPARATION GUIDE FOR USE WITH <Invented Name> 5 mg/ml CONCENTRATE

FOR SOLUTION FOR INFUSION

It is important that you read the entire contents of this procedure prior to the preparation of the <Invented Name> solution for infusion

1. FORMULATION

<Invented Name> 5 mg/ml concentrate for solution for infusion is a clear, colourless liquid containing 5 mg/ml oxaliplatin in water for injections.

2. PRESENTATION

<Invented Name> is supplied as single-dose vials. Each box contains one <Invented Name> vial (50 mg, 100 mg or200 mg).
The <Invented Name> 10 ml vial is a Type I clear glass of 50 mg oxaliplatin concentrate for solution for infusion with bromobutyl rubber stopper.
The <Invented Name> 20 ml vial is a Type I clear glass of 100 mg oxaliplatin concentrate for solution for infusion with bromobutyl rubber stopper.
The <Invented Name> 40 ml vial is a Type I clear glass of 200 mg oxaliplatin concentrate for solution forinfusion with bromobutyl rubber stopper.

<Invented Name> as packaged for sale:
This medicinal product does not require any special storage conditions.

Solution for infusion:
After dilution of the concentrate for solution for infusion in glucose 5% (50 mg/ml) solution, chemical and physical in-use stability has been demonstrated for 48 hours at 2°C to 8°C and for 24 hours at +25°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 (not to exceed 48 hours).

Inspect visually prior to use. Only clear solutions without particles should be used.
The medicine is for single use only. Any unused solution should be discarded.

3. RECOMMENDATIONS FOR THE 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 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 product, the protection of the environment and in particular the protection of the personnel handling the medicines, in accordance with the hospital policy. It requires a preparation area reserved for this purpose. It is forbidden to smoke, eat or drink in this area.

Personnel must be provided with appropriate handling materials, notably long sleeved gowns, protection masks, caps, protective goggles, sterile single-use gloves, protective covers for the work area, containers and collection bags for waste.

Excreta and vomit must be handled with care.

Pregnant women must be warned to avoid handling cytotoxic agents.

Any broken container must be treated with the same precautions and considered as contaminated waste. Contaminated waste should be incinerated in suitably labelled rigid containers. See below chapter "Disposal".

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

If oxaliplatin concentrate for solution for infusion or solution for infusion, 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 equipment containing aluminium.
- DO NOT administer undiluted.
- Only glucose 5% (50 mg/ml) 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 medicines in the same infusion bag or administer simultaneously by the same infusion line.
- DO NOT mix with alkaline medicines or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of others active substances. Alkaline medicines 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 givenat the same time as folinic acid intravenous infusion in glucose 5% (50 mg/ml) solution, over 2 to 6 hours, using a Y-line placed immediately before the site of infusion. These two medicines should not be combined in the same infusion bag. Folinic acid must not contain trometamol as an excipient and must only be diluted using isotonic glucose 5% (50 mg/ml) solution, never in alkaline solutions or sodium chloride or chloride containing solutions.

Instruction for use with 5-fluorouracil
Oxaliplatin should always be administered before fluoropyrimidines – i.e. 5-fluorouracil. Afteroxaliplatin administration, flush the line and then administer 5-fluorouracil.

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

- USE ONLY the recommended solvents (see below).

- Only clear solutions without particles should be used.

4.1 Preparation of the infusion solution

Withdraw the required amount of concentrate from the vial(s) and then dilute with 250 ml to 500 ml ofa glucose 5% (50 mg/ml) solution to give an oxaliplatin concentration between not less than 0.2 mg/ml and 0.7 mg/ml. The concentration range over which the physico-chemical stability of oxaliplatin hasbeen demonstrated is 0.2 mg/ml to 2.0 mg/ml.

Administer by intravenous infusion.

After dilution in glucose 5% (50 mg/ml) solution, chemical and physical in-use stability has been demonstrated for 48 hours at 2°C to 8°C and for 24 hour at +25°C.

From a microbiological point of view, this infusion preparation should be used immediately.
If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C unless dilution has taken place in controlled and validated aseptic conditions (not to exceed 48 hours).

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

The medicine is for single use only. Any unused infusion solution should be discarded (see chapter "disposal" below).

NEVER use sodium chloride or chloride containing solutions for dilution.

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

4.2 Infusion of the solution

The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 to 500 ml of a glucose 5% (50 mg/ml) 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.

4.3 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 in accordance with local requirements related to the disposal of hazardous waste