Package leaflet: Information for the patient

Oxaliplatin Ebewe, 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 further questions, please ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Oxaliplatin Ebewe is and what it is used for

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

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

Oxaliplatin Ebewe 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 Ebewe

You should not be given Oxaliplatin Ebewe:
- if you are **allergic** to oxaliplatin
- if you are **breast-feeding**
- 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 performing delicate tasks**, such as buttoning clothes
- if you have **severe kidney problems**

Warnings and precautions:
Talk to your doctor before you are given **Oxaliplatin Ebewe**

- 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

Inform your doctor immediately
- if you experience numbness or tingling in your fingers or toes or difficulty in swallowing. These symptoms can persist after the end of the treatment up to 3 years and may not be reversible. Your doctor will perform a neurological examination regularly, especially if other drugs are co-administered which affect the nerves.
- if you experience persistent or severe diarrhoea, nausea or vomiting.
- if you experience sore lips or mouth ulcers.
- if you have abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature. As oxaliplatin can cause a reduction of the number of blood cells, your doctor will check your blood frequently.
- if you experience unexplained respiratory symptoms such as a non-productive cough, difficulty in breathing or crackles.

Tell your doctor or your nurse immediately, if you notice a sensation of discomfort close to or at the injection site during the infusion (possible leakage into the surrounding tissue).

If you are pregnant or planning a pregnancy it is very important that you discuss this with your doctor before you receive any treatment. Oxaliplatin may have an anti-fertility effect, which could be irreversible. Male patients are therefore advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment. Male patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 6 months.

Children
There is no relevant indication for use of oxaliplatin in children. The safety and efficacy of oxaliplatin in children has not been established.

Other medicines and Oxaliplatin Ebewe
Tell your doctor if you are using, have recently used or might use any other medicines.

Pregnancy, breast-feeding and fertility
You must not be treated with oxaliplatin during pregnancy unless clearly indicated by your doctor. It is therefore important to tell your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.

You must not become **pregnant** during treatment with oxaliplatin and must use an effective method of contraception. If pregnancy occurs during your treatment, you must immediately inform your doctor. You should take appropriate contraceptive measures during and after cessation of therapy continuing for 4 months for women and 6 months for men.

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

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

Driving and using machines
Oxaliplatin treatment may result in an increase risk of dizziness, nausea and vomiting, and other neurological symptoms that affect gait and balance. These can influence your ability to drive and use machines, so do not do either until you are sure of how Oxaliplatin affects you. If you have vision

problems while taking Oxaliplatin, do not drive, operate heavy machines, or engage in dangerous activities.

3. How Oxaliplatin Ebewe is used

This medicine will be administered by medical personnel; do not take it yourself.
Oxaliplatin Ebewe is intended in adults only.

Dosage

The dose of Oxaliplatin Ebewe is based on your body surface area. This is calculated from your height and weight.
The usual dose for adults including the elderly is 85 mg/m^2 of body surface area. The dose you receive will also depend on results of blood tests and whether you have previously experienced side effects with Oxaliplatin Ebewe.

Method and route of administration

- **Oxaliplatin Ebewe** 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 Ebewe**.
- Oxaliplatin Ebewe 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 Ebewe 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 Ebewe 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 Ebewe 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:

- Persistent or severe diarrhoea or vomiting
- Presence of blood or dark brown coffee-coloured particles in your vomit
- 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).
- Stomatitis/mucositis (sore lips or mouth ulcers)
- Swelling of the face, lips, mouth or throat
- Unexplained respiratory symptoms such as non-productive cough, difficulty in breathing or crackles
- Difficulty in swallowing
- Numbness or tingling in your fingers or toes
- Extreme tiredness
- Abnormal bruising or bleeding
- Signs of infection, such as sore throat and high temperature
- Sensation of discomfort close to or at the injection site during the infusion.

Known side effects of Oxaliplatin Ebewe:

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

- A disorder of the nerves which can cause weakness, tingling or numbness in the fingers, toes, around the mouth or in the throat that may sometimes occur in association with cramps. This is 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 completely there is a possibility of persistent symptoms after the end of the treatment
- A tingling shock-like sensation passing down the arms or chest when the neck is flexed (Lhermitte´s sign)
- 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 usually subsides without the need for any treatment
- Jaw spasm, abnormal tongue sensation, possibly affecting speech, and a feeling of chest pressure. Your doctor may decide to alter your treatment as a result
- Taste alteration
- Headache
- Sore throat and high temperature (signs of infection)
- Reduction in the number of white blood cells, which make infections more likely
- Reduction in red blood cells, which can make the skin pale and cause weakness or breathlessness
- Reduction in blood platelets, which increases risk of bleeding or bruising
- Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course.

- Nosebleeds
- Allergic reactions - skin rash including red itchy skin, inflammation of the conjunctiva, swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint
- Shortness of breath, coughing
- Loss or lack of appetite
- Nausea (feeling sick), vomiting (being sick) - medication to prevent sickness is usually given to you by your doctor before treatment and may be continued after treatment.
- Diarrhoea, if you suffer from persistent or severe diarrhoea or vomiting, contact your doctor immediately for advice.
- Sore mouth or lips, mouth ulcers
- Stomach pain, constipation
- Skin disorder
- Hair loss
- Back pain
- Tiredness, loss of strength/weakness, body pain
- Pain or redness close to or at the injection site during the infusion
- Fever
- Weight gain
- High levels of glucose (sugar) in your blood, which may cause a great thirst, dry mouth or a need to urinate more often
- Rigors (tremors)
- Low blood levels of potassium, which can cause abnormal heart rhythm and can be recognised by muscle cramps, muscle weakness or fatigue.
- High levels of blood sodium which can cause confusion, muscle twitching or abnormal heart rhythm.
- Abnormal blood tests which show changes of liver function (increase of alkaline phosphatase, bilirubin, LDH and hepatic enzymes)

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

- Reduction in the number of a special form of white blood cells accompanied by fever and/or generalized infection / infections of the respiratory tract
- Dehydration
- Depression
- Difficulty sleeping
- Dizziness
- Inflammation of nerves leading to muscle spasms, cramps, loss of certain reflexes
- Neck stiffness, intolerance/dislike of bright light and headache
- Conjunctivitis, visual problems
- Abnormal bleeding, blood in the urine and stools
- Presence of blood or dark brown coffee-coloured particles in your vomit
- Blood clot, usually in a leg, which causes pain, swelling or redness
- Blood clot in the lungs which causes chest pain and breathlessness
- Runny nose
- Upper respiratory tract infection
- Flushing
- Chest pain, hiccups
- Indigestion and heartburn
- Loss of weight
- Peeling skin, skin rash, increased sweating and nail disorder

- Joint pain and bone pain
- Pain on passing urine or a change in frequency when passing urine
- Abnormal blood tests which show changes of kidney function (e.g. increase of creatinine)
- High blood pressure

Uncommon (may affect up to 1 in 100 people)**:**
- Nervousness
- Hearing problems (ototoxicity)
- Impaired or blocked bowel passage
- Disturbance in the body's acid-base balance

Rare (may affect up to 1 in 1,000 people)**:**
- Reduction in blood platelets due to an allergic reaction associated with bruises and abnormal bleeding (immunoallergic thrombocytopenia)
- Reduction in red blood cells caused by cell destruction
- Slurred speech
- Temporary fall in visual acuity; visual field disturbances, reversible short-term vision loss
- Deafness
- Unexplained respiratory symptoms, difficulties in breathing, scarring of the lungs which causes shortness of breath, sometimes fatal
- Bowel inflammation causing abdominal pain or diarrhoea, including severe bacterial infection (Clostridium difficile)
- Inflammation of the optic nerve
- Pancreatitis

Very rare (may affect up to 1 in 10,000 people)**:**
- Liver disease that your doctor will monitor you for
- Changes in kidney function

Frequency not known (cannot be estimated from the available data)**:**
- Convulsion.

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 IMB Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Oxaliplatin Ebewe

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

Oxaliplatin Ebewe 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.

Do not use this medicine after the expiry date which is stated on the carton and the label. 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 Ebewe contains
- The active substance is Oxaliplatin.
- The other ingredients are Lactose monohydrate and Water for injections

What Oxaliplatin Ebewe 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 contains 50 mg of oxaliplatin.
20 ml of concentrate for solution for infusion contains 100 mg of oxaliplatin.
30 ml of concentrate for solution for infusion contains 150 mg of oxaliplatin.
40 ml of concentrate for solution for infusion contains 200 mg of oxaliplatin.

Pack sizes:
50mg/10ml: 1 vial, 5 vials, 10 vials
100mg/20ml: 1 vial
150mg/30ml: 1 vial
200mg/40ml: 1 vial

With or without a protective plastic overwrap (Onco-Safe).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

EbewePharmaGes.m.b.HNfg.KG
Mondseestrasse11
4866Unterach
Austria

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

AT: Oxaliplatin Ebewe 5mg/ml Konzentrat zur Herstellung einer Infusionslösung
BE: Oxaliplatin Sandoz 5 mg/ml concentraat voor oplossing voor infusie
BG: Oxaliplatin Ebewe 5mg/ml concentrate for solution infusion

CZ: Oxaliquid 5 mg/ml
DK: Oxaliplatin "Sandoz"
EE: Oksaliplatiin „Ebewe“ 5 mg/ml
ES: Oxaliquid 5 mg/ml concentrado para solución para perfusión
FI: Oxaliplatin Sandoz 5 mg/ml infuusiokonsentraatti, liuosta varten
FR: OXALIPLATINE SANDOZ 5 mg/ml, solution à diluer pour perfusion
Greece : PLAXITIN, 5mg/ml, πυκνό διάλυμα για παρασκευή διαλύματος προς έγχυση
IE : Oxaliplatin Ebewe 5mg/ml concentrate for solution for infusion
IT: Oxaliplatino Sandoz
LV: OXALIPLATIN EBEWE 5 mg/ml koncentrāts infūziju šķīduma pagatavošanai
LT: Oksaliplatina EBEWE 5mg/ml koncentratas infuziniam tirpalui
MT: Oxaliplatin Ebewe 5 mg/ml concentrate for solution for infusion
NL: Oxaliplatine Sandoz concentraat 5 mg/ml, concentraat voor oplossing voor infusie
NO: Oxaliplatin Sandoz 5 mg/ml konsentrat til infusjonsvæske, oppløsning
PL: Oxaliplatin-Ebewe
PT: Oxaliplatina Tubernax
RO: Oxaliplatin Ebewe 5 mg/ml, concentrat pentru soluţie perfuzabilă
SK: Oxaliplatin Sandoz 5 mg/ml infúzny koncentrát
SI: Oksaliplatin Ebewe 5 mg/ml koncentrat za raztopino za infundiranje
ES: Oxaliquid 5 mg/ml concentrado para solución para perfusión
SE: Oxaliplatin Sandoz 5 mg/ml koncentrat till infusionsvätska, lösning.
GB: Oxaliplatin 5 mg/ml Concentrate for Solution for Infusion

This leaflet was last revised in 04/2014

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 0.2 mg/ml.

Administer by IV 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 48 hours at 2 to 8 °C when diluted to the concentrations of 0.2 mg/ml and 2.0 mg/ml with glucose 5% as well as for 6 hours at 20-25 °C when diluted to the concentration of 0.2 mg/ml and 2.0 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 either reconstitution or dilution.

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.

Disposal

Remnants of the medicinal product as well as all materials that have been used for reconstitution, 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.

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: 18 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 48 hours at 2 to 8 °C when diluted to the concentrations of 0.2 mg/ml and 2.0 mg/ml with glucose 5% as well as for 6 hours at 20-25 °C when diluted to the concentration of 0.2 mg/ml and 2.0 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.