Package leaflet: Information for the patient

Oxaliplatin Ebewe 5mg/ml powder 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.

What is in this leaflet:

1. **What** Oxaliplatin Ebewe 5mg/ml powder for solution for infusion **is and what it is used for**

Oxaliplatin Ebewe 5mg/ml powder for solution for infusion is an anticancer medicine and contains the active substance oxaliplatin.

Oxaliplatin Ebewe 5mg/ml powder for solution for infusion is used **to treat cancer of the large** bowel **(treatment of stage III colon** cancer after **complete resection of primary tumour, metastatic cancer of colon and rectum).**

Oxaliplatin Ebewe 5mg/ml powder for solution for infusion 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 5mg/ml powder for solution for infusion

You should not be given Oxaliplatin Ebewe 5mg/ml powder for solution for infusion**:**

1. if you are **allergic** to oxaliplatin
2. if you are **breast-feeding**
3. if you already have a **reduced number of blood cells**
4. if you already have **tingling and numbness in the fingers and/or toes**, and have **difficulty performing delicate tasks**, such as buttoning clothes
5. if you have **severe kidney problems**

Warnings and precautions:
Talk to your doctor before you are given Oxaliplatin Ebewe 5mg/ml powder for solution for infusion

- 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

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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)

Vaccination during therapy with Oxaliplatin may lack the required effect and can result in serious or fatal infections. Vaccination should be avoided if you receive Oxaliplatin. Please talk to your doctor for any vaccination required during Oxaliplatin therapy.

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 5mg/ml powder for solution for infusion
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 5mg/ml powder for solution for infusion **is used**

This medicine will be administered by medical personnel; do not take it yourself.
Oxaliplatin Ebewe 5mg/ml powder for solution for infusion is intended in adults only.

Dosage

The dose of Oxaliplatin Ebewe 5mg/ml powder for solution for infusion 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 5mg/ml powder for solution for infusion.

Method and route of administration

- Oxaliplatin Ebewe 5mg/ml powder for solution for infusion 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 5mg/ml powder for solution for infusion.
- Oxaliplatin Ebewe 5mg/ml powder for solution for infusion 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 5mg/ml powder for solution for infusion 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 5mg/ml powder for solution for infusion **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 5mg/ml powder for solution for infusion **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:

- you may feel you are going to faint (signs of allergic reactions may occur in minutes - sometimes fatal). Signs are: 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)
- 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)
- Unexplained respiratory symptoms such as non-productive cough, crackles
- 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.

Other side effects of Oxaliplatin Ebewe 5mg/ml powder for solution for infusion **are**:

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, 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
- headache, confusion, seizures and visual loss (Reversible Posterior Leukoencephalopathy syndrome (RPLS))

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.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store Oxaliplatin Ebewe 5mg/ml powder for solution for infusion

Oxaliplatin Ebewe 5mg/ml powder for solution for infusion **should not come into contact with the eyes or skin. If there is any accidental spillage, tell the doctor or nurse immediately.**

Keep out of the sight and reach of children.

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

This medicinal product does not require any special storage conditions.

Reconstituted concentrate solution in the original vial:
The reconstituted concentrate solution should be diluted immediately.

Solution for infusion after dilution:
After dilution of the reconstituted solution in glucose 5 % solution, chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°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.

6. Contents of the pack and other information

What Oxaliplatin „Ebewe“ contains
- The active substance is oxaliplatin.

50 mg vial: Each vial contains 50 mg oxaliplatin for reconstitution in 10 ml of solvent.
100 mg vial: Each vial contains 100 mg oxaliplatin for reconstitution in 20 ml of solvent.
150 mg vial: Each vial contains 150 mg oxaliplatin for reconstitution in 30 ml of solvent.

One ml of the reconstituted concentrate solution contains 5 mg oxaliplatin.

- The other ingredient is lactose monohydrate

What Oxaliplatin „Ebewe“ looks like and contents of the pack
This medicinal product is a powder for solution for infusion.
Each vial contains a white to off-white powder for solution for infusion containing 50 mg, 100 mg or 150 mg oxaliplatin. The vials are supplied in cartons of one (1).

Oxaliplatin „Ebewe“ has to be dissolved and made into a solution before it can be injected into a vein.

Marketing Authorisation Holder and Manufacturer:

EBEWE Pharma Ges.m.b.H. Nfg.KG
A-4866 Unterach,
AUSTRIA

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The following information is intended for healthcare professionals only:

Special precautions for disposal
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 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 powder, reconstituted solution or infusion solution should come into contact with skin, wash immediately and thoroughly with water.
If oxaliplatin powder, reconstituted solution or infusion solution 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 (50 mg/ml) is to be used as a diluent.
- DO NOT reconstitute or dilute for infusion with sodium chloride or chloride containing solutions.
- DO NOT administer extravascularly.
- DO NOT mix with any other medication in the same infusion bag or administer simultaneously by the same infusion line.

- DO NOT mix with alkaline drugs or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of other drugs. Alkaline drugs or solutions will adversely affect the stability of oxaliplatin.

Instruction 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 (50 mg/ml) 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 drugs 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.
Any reconstituted solution that shows evidence of precipitation should not be used and should be destroyed with due regard to legal requirements for disposal of hazardous waste (see below).
Reconstitution of the powder

- Water for injections or 5 % glucose solution (50 mg/ml) should be used to reconstitute the solution.
- For a vial of 50 mg: add 10 ml of solvent to obtain a concentration of 5 mg oxaliplatin/ml.
- For a vial of 100 mg: add 20 ml of solvent to obtain a concentration of 5 mg oxaliplatin/ml.
- For a vial of 150 mg: add 30 ml of solvent to obtain a concentration of 5 mg oxaliplatin/ml.

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 (see below "Disposal").

Dilution before infusion

Withdraw the required amount of reconstituted concentrate 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 not less than 0.2 mg/ml and 0.7 mg/ml, concentration range for which the physico-chemical stability of oxaliplatin has been demonstrated.
Administer by IV infusion.
After dilution in 5% glucose, chemical and physical in-use stability has been demonstrated for 24 hours at +2°C to +8°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.
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 solution for either reconstitution or dilution.
The compatibility of Oxaliplatin solution for infusion has been tested with representative, PVC-based, administration 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.

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 with due regard to current laws related to the disposal of hazardous waste.