Package leaflet: Information for the user

Oxaliplatin medac 5 mg/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 any further questions, ask your doctor, 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

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

Oxaliplatin medac is an anticancer drug and contains platinum. Oxaliplatin medac 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 medac is used in combination with other anticancer medicines called 5-fluorouracil and folinic acid.

2. What you need to know before you are given Oxaliplatin medac

You should not be given Oxaliplatin medac:
- if you are allergic to oxaliplatin or any of the other ingredients of this medicine (listed in section 6).
- 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, pharmacist or nurse before you are given Oxaliplatin medac
- if you have ever suffered an allergic reaction to platinum-containing medicines such as carboplatin or cisplatin.
- if you have moderate kidney problems.
- 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 experience 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.
- if you also receive 5-fluorouracil, because the risk of diarrhoea, vomiting, sore mouth and blood abnormalities is increased.
- if you notice a sensation of discomfort close to or at the injection site during the infusion (possible leakage into the surrounding tissue).

Other medicines and Oxaliplatin medac
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you start a therapy with this medicine.

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 during 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
Since oxaliplatin treatment may result in an increased risk of dizziness, nausea and vomiting, and other neurological symptoms that affect gait and balance, it may lead to a minor or moderate influence on your ability to drive and use machines.
Vision abnormalities, in particular transient vision loss (reversible following therapy discontinuation), may also affect your ability to drive and use machines.

3. How Oxaliplatin medac is given

Oxaliplatin medac is only to be given to adults.

Oxaliplatin medac will be prescribed for you by a specialist in cancer treatment. You will be treated under medical supervision.

Oxaliplatin medac is given by injection into a vein (an intravenous infusion) over a 2 to 6 hour period. The injection is made by mixing the powder with water for injections or 5 % glucose. This solution is then diluted further in 5 % glucose. Oxaliplatin medac will be made up by a healthcare professional.

The dose of Oxaliplatin medac is based on your body surface area. This is calculated from your height and weight.

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

The dose you receive will also depend on results of blood tests and whether you have previously experienced side effects with Oxaliplatin medac.

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 Oxaliplatin medac than you should:
Your doctor will ensure that the correct dose for your condition is given. In case of overdose, you may experience increased side effects. Your doctor may give you symptomatic treatment for these side effects.

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.
- Persistent or severe diarrhoea or vomiting
- 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
- Low urine output (or no urine output)
- Signs of infection, such as sore throat and high temperature
- Sensation of discomfort close to or at the injection site during the infusion

Very common side effects (in more than 1 of 10 patients):
- 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.
- Some people have experienced a tingling shock-like sensation passing down the arms or trunk when the neck is flexed.
- Oxaliplatin can sometimes cause an unpleasant sensation in the throat, in particular when swallowing, and give the sensation of shortness of breath. This sensation, if it happens, usually occurs during or within hours of the infusion and may be triggered by exposure to the cold. Although unpleasant, it will not last long and usually subsides without the need for any treatment. Jaw spasm, abnormal tongue sensation, possibly affecting speech, and a feeling of chest pressure have also been reported. Your doctor may decide to alter your treatment as a result.
- Taste disorder
- Headache
- Signs of infection such as a sore throat and high temperature.
- 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
- Abnormal levels of glucose (sugar) in your blood e.g. too high levels which may cause a great thirst, dry mouth or a need to urinate more often
- Low blood levels of potassium which can cause abnormal heart rhythm
- Abnormal levels of sodium blood levels e.g. low sodium levels which can cause tiredness and confusion, muscle twitching, fits or coma
- Abnormal blood tests which show changes of liver function (increase of alkaline phosphatase, bilirubin, LDH and hepatic enzymes)

Common side effects (in less than 1 in 10 but more than 1 in 100 patients):
- Serious allergic reactions which cause difficulties in breathing, rash, swelling of the face, tongue or throat and low blood pressure
- Reduction in the number of a special form of white blood cells accompanied by fever and/or generalized infection
- 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
- 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)
- Fall

Uncommon side effects (in less than in 1 in 100 but more than 1 in 1,000 patients):
- Nervousness
- Hearing problems
- Impaired or blocked bowel passage
- Disturbance in the body's acid-base balance

Rare side effects (in less than 1 in 1,000 but more than 1 in 10,000 patients):
- Reduction in blood platelets due to an allergic reaction
- Reduction in red blood cells caused by cell destruction
- Slurred speech
- Reversible posterior leukoencephalopathy syndrome (a syndrome characterised by headache, dizziness, seizures, high blood pressure and visual disturbances)
- Temporary fall in visual acuity; visual field disturbances, transient vision loss
- Inflammation of the optic nerve
- Deafness
- Unexplained respiratory symptoms, difficulties in breathing, scarring of the lungs which causes shortness of breath
- Bowel inflammation causing abdominal pain or diarrhoea, including severe bacterial infection (*Clostridium difficile*)
- Inflammation of the pancreas, which causes severe pain in the abdomen and back

Very rare effects (in less than 1 in 10,000 patients):
- Liver disease that your doctor will monitor you for
- Changes in kidney function, kidney failure

Not known (frequency cannot be estimated from the available data)
- Convulsion
- Allergic vasculitis (inflammation of blood vessels)
- Auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia)
- 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)

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.

Oxaliplatin medac should not come into contact with the eyes or skin. If there is any accidental spillage, tell the doctor or nurse immediately.

5. How to store Oxaliplatin medac

Keep this medicine 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 medac 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 medac 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 medac has to be dissolved and made into a solution before it can be injected into a vein.

Marketing Authorisation Holder and Manufacturer

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

Cyprus	Οξαλιπλατίνη medac
Finland, Ireland	Oxaliplatin medac
Germany	Medoxa®

This leaflet was last revised in February 2019.

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 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 85 mg/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.