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. See section 4.

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 have any liver problems or abnormal liver function test results during your treatment.
- 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 any of the following applies to you at any time, tell your doctor immediately. Your doctor may need to treat you for these events. Your doctor may need to reduce the dose of Oxaliplatin medac, or delay or stop your treatment with Oxaliplatin medac.

- If you have an unpleasant sensation in the throat, in particular when swallowing, and have a sensation of shortness of breath, during the treatment, tell your doctor.
- If you have nerve problems in your hands or feet, such as numbness or tingling, or decreased sensations in your hands or feet, tell your doctor.
- If you have headache, altered mental functioning, seizures and abnormal vision from blurriness to vision loss, tell your doctor.
- If you feel or are sick (nausea or vomiting), tell your doctor.
- If you have severe diarrhoea, tell your doctor.
- If you have sore lips or mouth ulcers (mucositis/ stomatitis), tell your doctor.
- If you have diarrhoea, or a reduction in white blood cells or platelets, tell your doctor. Your doctor may reduce the dose of Oxaliplatin medac or postpone your treatment with Oxaliplatin medac.
- If you have unexplained respiratory symptoms such as cough, or any difficulties in breathing, tell your doctor. Your doctor may stop your treatment with Oxaliplatin medac.
- If you develop an extreme tiredness, shortness of breath, or kidney disease where you pass little or no urine (symptoms of acute renal failure), tell your doctor.
- If you have fever (temperature greater than or equal to 38°C), or chills, which could be signs of infection, tell your doctor immediately. You may be at risk of getting an infection of the blood.
- If you have fever > 38°C, tell your doctor. Your doctor may determine you also have a reduction in white blood cells.
- If you experience unexpected bleeding or bruising (disseminated intravascular coagulation), tell your doctor as these could be signs of blood clots throughout the small vessels of your body.
- If you faint (lose consciousness) or have an irregular heartbeat while taking Oxaliplatin medac, tell your doctor immediately as this may be a sign of a serious heart condition.
- If you experience muscle pain and swelling, in combination with weakness, fever, or red-brown urine, tell your doctor. These could be signs of muscle damage (rhabdomyolysis) and could lead to kidney problems or other complications.
- If you have abdominal pain, nausea, bloody vomit or vomit that looks like “coffee-grounds”, or dark-colored/ tarry stools, which may be signs of an ulcer of the bowel (gastrointestinal ulcer, with potential bleeding or perforation), tell your doctor.
- If you have abdominal (tummy) pain, bloody diarrhea, and nausea and/or vomiting, which may be caused by a reduction of blood flow to your gut wall (intestinal ischaemia), tell your doctor.

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 taking this medicine.

Pregnancy
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.

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 and up to 6 months after treatment and to take appropriate contraceptive measures during this time.

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 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)
- Unexplained respiratory symptoms such as non-productive cough, difficulty in breathing or crackles
- Abnormal bruising or bleeding

- Signs of infection, such as sore throat and high body temperature
- 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)
- 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)
- Presence of blood or dark brown coffee-coloured particles in your vomit

Other side effects include:

Very common (may affect more than 1 in 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
- 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.
- Skin pallor, weakness, and breathlessness
- 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
- 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 (extravasation)
- 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. high 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 (may affect up to 1 in 10 patients):
- Reduction in the number of a special form of white blood cells accompanied by fever and/or generalized infection
- Serious infection of the blood in addition to a reduction in white blood cells (neutropenic sepsis), which may be fatal
- 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)
- Reduction in white blood cells accompanied by fever > 38.3°C or a prolonged fever > 38°C for more than one hour (febrile neutropenia)
- Decreased levels of calcium in the blood
- High blood pressure
- Fall

Uncommon (may affect up to 1 in 100 patients):
- Nervousness
- Hearing problems
- Impaired or blocked bowel passage
- Disturbance in the body's acid-base balance
- Serious infection of the blood (sepsis), which may be fatal

Rare (may affect up to 1 in 1,000 patients):
- Reduction in blood platelets due to an allergic reaction
- Reduction in red blood cells caused by cell destruction
- Slurred speech
- 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 (may affect up to 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)
- Reduction of all blood cell lines (pancytopenia)
- Auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia)
- Cancer of white blood cells (secondary leukaemia)
- 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)
- Serious infection of the blood and low blood pressure (septic shock), which may be fatal
- Abnormal heart rhythm (QT prolongation), that can be seen on electrocardiogram (ECG), which may be fatal
- Spasm of the throat causing difficulty in breathing
- Decreased blood flow to the intestine/bowel (intestinal ischaemia), which may be fatal
- Abdominal pain, nausea, bloody vomit or vomit that looks like "coffee grounds", or dark-colored/tarry stools (symptoms of gastrointestinal ulcer, with potential bleeding or perforation), which may be fatal
- Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal
- Obstruction or bleeding of the brain
- Inflammation of the lung and airways, which may be fatal

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, Website: www.hpra.ie. By reporting side affects 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, Finland, Ireland	Oxaliplatin medac
Germany	Medoxa®

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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.