Package leaflet: Information for the user

Oxaliplatin medac 5 mg/ml concentrate for solution for infusion
oxaliplatin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. 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

The active ingredient of Oxaliplatin medac is oxaliplatin.

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.

Oxaliplatin medac is an antineoplastic or anticancer medicine and contains platinum.

2. What you need to know before you use Oxaliplatin medac

Do not use Oxaliplatin medac
- if you are allergic to oxaliplatin or any of the other ingredients of this medicine (listed in section 6).
- if you are breastfeeding.
- 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 or pharmacist before using Oxaliplatin medac

- if you have ever suffered an allergic reaction to platinum-containing medicines (e.g. carboplatin or cisplatin). Allergic reactions can occur during any oxaliplatin infusion.
- if you have moderate or mild 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 you have recently received or plan to receive any vaccines. During treatment with oxaliplatin, you should not have a vaccination with “live” or “attenuated” vaccines, such as yellow fever vaccine.

If 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-coloured/ 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 diarrhoea, 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, breastfeeding and fertility

Pregnancy
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
If you are pregnant or planning a pregnancy it is very important that you discuss this with your doctor **before** you receive any treatment.
If you get pregnant during your treatment, you must immediately inform your doctor.

Contraception for men and women

Men
Male patients are advised not to father a child during treatment and until 6 months after treatment, and have to use effective contraception during this time.

Women
It is not recommended that you become pregnant during treatment with oxaliplatin. Female patients have to use effective contraception during and after therapy continuing for 9 months.

Breastfeeding
You must not breastfeed while on treatment with Oxaliplatin medac.

Fertility
Oxaliplatin may have an anti-fertility effect, which could be irreversible. Male patients should seek advice on conservation of sperm prior to treatment.

Driving and using machines
Treatment with Oxaliplatin medac involves an increased risk of dizziness, nausea and vomiting, and other neurological symptoms that affect walking and balance. If this happens you should not drive or operate machinery. If you have vision problems while taking this medicine, do not drive, operate machinery or engage in potentially dangerous activities.

3. How to use Oxaliplatin medac

Oxaliplatin medac may only be administered to adults.
For single use only.

Dose
The dose depends on the body surface area (calculated in m^2), which is determined from your height and weight. In addition the dose depends on the results of blood tests and whether you have previously experienced side effects with oxaliplatin.

The recommended dose for adults, including elderly patients, is 85 mg/m^2 body surface area.

Route of administration
Oxaliplatin medac will be prescribed to you by a doctor with experience in the treatment of cancer.
You will be treated by a healthcare professional, who will have made up the required dose of Oxaliplatin medac.
Oxaliplatin medac is given by slow injection into a vein (intravenous infusion) over a 2 to 6 hour period.
Oxaliplatin medac 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 use
The duration of therapy will be decided by your doctor.
Your treatment will last a maximum of 6 months when used after complete removal of your tumour.

If you use more Oxaliplatin medac than you should
As this medicine is administered by a healthcare professional, it is highly unlikely that you have received too much or too little. However, do inform your doctor if you have any concerns.
In case of overdose, you may experience increased side effects. Your doctor will give you appropriate 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.

Please inform your doctor immediately if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- 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.
- Abnormal occurrence of bruises, bleeding, or signs of infection such as a sore throat or a high body temperature.
- Persistent or severe diarrhoea or vomiting.
- Sore lips or mouth ulcers (stomatitis/mucositis).
- Unexplained respiratory symptoms such as dry cough, difficulty in breathing or crackles.

Common: may affect up to 1 in 10 people
- Serious infection of the blood in addition to a reduction in white blood cells (neutropenic sepsis), which may be fatal.

Uncommon: may affect up to 1 in 100 people
- Serious infection of the blood (sepsis), which may be fatal.

Rare: may affect up to 1 in 1,000 people
- A group of symptoms such as headache, altered mental functioning, seizures and abnormal vision from blurriness to vision loss (symptoms of reversible posterior leukoencephalopathy syndrome, a rare neurological disorder).
- 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).

Very rare: may affect up to 1 in 10,000 people
- Presence of blood or dark brown coffee-coloured particles in your vomit.

Not known: frequency cannot be estimated from the available data
- Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal.

Other side effects include:

Very common: may affect more than 1 in 10 people
- Oxaliplatin can affect the nerves (peripheral neuropathy). You may feel a tingling and/or numbness in the fingers, toes, around the mouth, or in the throat, which may sometimes occur in association with cramps. These symptoms are often provoked by exposure to cold, for example by opening the refrigerator or holding a cold drink. You may also experience difficulties with the performance of fine motor movements such as buttoning up clothing. Even though in the majority of cases these symptoms disappear completely, there is a possibility that they will persist 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 may sometimes cause an unpleasant sensation in the throat, which is especially noticeable on swallowing and which gives an impression of shortness of breath. If this occurs, it usually does so during or within a few hours after the end of the infusion, and is triggered by exposure to cold. This unpleasant phenomenon does not last long and regresses without needing any treatment. Your doctor will decide on any adjustment of treatment.

- Oxaliplatin causes temporary reduction in the number of blood cells. The reduction of red cells may cause anaemia (a reduction of red cells), abnormal bleeding or bruising (due to a reduction in platelets). The reduction in white blood cells may make you prone to infections. Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course.
- An increased risk of bleeding and occurrence of extravasation (leaking of fluid into the surrounding tissue).
- Skin pallor, weakness, and breathlessness.
- Complete or partial loss of appetite.
- High levels of blood glucose (blood sugar), which can cause a strong thirst, a dry mouth, or an increased frequency of passing urine.
- Irregular heartbeat (caused by a low level of potassium in blood).
- Tiredness, disorientation, muscle twitching, cramp attacks, and profound coma (caused by a high level of sodium in blood).
- Disturbances of the sense of taste.
- Headaches.
- Nosebleeds.
- Nausea and vomiting – to avoid these effects you will usually be given medication by your doctor before, and if necessary, also after the treatment.
- Swelling of the nerves to your muscles, neck stiffness, abnormal tongue sensation possibly altering speech.
- Abdominal pains, constipation.
- Skin disorders.
- Loss of hair.
- Backache.
- Tiredness, loss of strength, sensation of weakness, pains in the whole body.
- Pain or skin reddening both around and directly at the injection site during the infusion.
- Fever, rigors (tremors).
- Alteration in blood tests including those relating to abnormalities in liver function.
- Weight gain.

Common: may affect up to 1 in 10 people
- Infection due to a reduction in white blood cells.
- Inflammation of nasal mucous membranes.
- Respiratory tract infection.
- Loss of fluid with tissue dehydration.
- Pronounced excitability and irritability.
- Dizziness.
- Swelling of muscle-supplying nerves.
- Stiff neck, light intolerance, aversion to dazzling light, headaches.
- Conjunctivitis, visual disturbances.
- Abnormal bleeding, blood in urine or stool.
- Blood clot formation, usually in a leg, with painful swelling and reddening.
- Blood clot in the lung, causing chest pains and breathlessness.
- Attacks of skin reddening.
- Pains in the chest, hiccups.
- Digestive disturbances, heartburn.
- Peeling skin, rash, increased sweating and nail disorders.
- Pains in the joints and bones.
- Pains when passing urine or a change in urination frequency.
- Blood tests showing a change in kidney function.
- Loss of weight.
- Depression.
- Sleep disturbances.
- 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 people
- Hearing disturbances.
- Blockage or swelling of the bowel.
- Anxiety or nervousness.
- Higher acidity of the blood.

Rare: may affect up to 1 in 1,000 people
- Indistinct speech.
- Deafness.
- Scarring and thickening in the lungs with difficulties in breathing, sometimes fatal (interstitial lung disease).
- Inflammations causing abdominal pains and diarrhoea.
- Reversible short-term loss of vision.
- Unexpected bleeding or bruising due to widespread blood clots throughout the small blood vessels of the body (disseminated intravascular coagulation), which may be fatal.

Very rare: may affect up to 1 in 10,000 people
- Liver disorders, for which your doctor will be watching out.
- Changes in kidney function where you pass little or no urine.

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).
- Reduction of all blood cell lines (pancytopenia).
- Blood cancer (secondary leukaemia).
- 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.
- Myocardial infarction (Heart attack), angina pectoris (pain or uncomfortable feeling in the chest).
- Spasm of the throat causing difficulty in breathing.
- Inflammation of the lung and respiratory system which may be fatal.
- 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-coloured/tarry stools (symptoms of gastrointestinal ulcer, with potential bleeding or perforation), which may be fatal.
- Oesophageal inflammation (inflammation of the lining of the oesophagus - the tube that connects your mouth with your stomach- resulting in pain and swallowing difficulty).
- Decreased blood flow in or bleeding of the brain.
- Non-cancerous abnormal liver nodules (focal nodular hyperplasia)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

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 label and the carton after EXP. The expiry date refers to the last day of that month.

Prior to mixing keep this medicine in the outer carton in order to protect from light. Store between 15 °C and 25 °C. Do not freeze.

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

This medicine is for single use only. When the infusion has finished, Oxaliplatin medac will be disposed carefully by the doctor or healthcare professional.

After dilution in 5 % glucose solution, chemical and physical in-use stability has been demonstrated for 48 hours at +2 °C to +8 °C and for 6 hours at +25 °C.
From a microbiological point of view, the infusion preparation should be used immediately.
If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C unless dilution has taken place in controlled and validated aseptic conditions.

6. Contents of the pack and other information

What Oxaliplatin medac contains

- The active substance is oxaliplatin. 1 ml of the concentrate for solution for infusion contains 5 mg oxaliplatin.
  Each vial of 10 ml of concentrate contains 50 mg oxaliplatin.
  Each vial of 20 ml of concentrate contains 100 mg oxaliplatin.
  Each vial of 40 ml of concentrate contains 200 mg oxaliplatin.
- The other ingredient is water for injections.

What Oxaliplatin medac looks like and contents of the pack

Oxaliplatin medac is a clear, colourless concentrate for solution for infusion.

Pack sizes
Packs with 1 vial containing 10 ml, 20 ml or 40 ml of concentrate for solution for infusion.

Marketing Authorisation Holder and Manufacturer:

medac Gesellschaft für Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Germany: medoxa
France: OXALIPLATINE MEDAC
United Kingdom: Oxaliplatin medac

This leaflet was last revised in 01/2023.

The following information is intended for healthcare professionals only:

Handling instructions for safe use
Like other potentially toxic substances, oxaliplatin solutions must be prepared and handled with due care.

The handling of this cytotoxic agent by medical health care professionals requires all safety measures ensuring protection of the user and his/her environment.

Injection solutions of cytotoxic medicinal products must be prepared by specially trained personnel familiar with the medicinal product used, under conditions guaranteeing the integrity of the medicinal product, protection of the environment, and especially protection of the personnel involved in accordance with the hospital's standard procedures. This requires the provision of a working area designated for this purpose, in which smoking, eating, and drinking are prohibited.

The personnel must be provided with suitable working equipment, and in particular with long-sleeve laboratory coats, protective masks, head coverings, protective goggles, sterile disposable gloves, protective workplace coverings, containers, and collection bags for waste.
Excrement and vomit must be handled with care.

Pregnant women must be warned against handling cytotoxic substances and must avoid them.

Any broken containers must be handled with the same care and treated as contaminated waste. Contaminated waste should be placed in solid suitably labeled containers for disposal by incineration. See below chapter "Waste disposal".

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

Preparation for the intravenous administration
Special precautions for use
- The product MUST NOT be used with aluminum-containing injection equipment.
- The product MUST NOT be administered undiluted.

Only glucose 5 % (50 mg/ml) infusion solution is to be used as a diluent.
- The product MUST NOT be diluted with sodium chloride or chloride-containing solutions.
- The product MUST NOT be mixed with any other medicinal products in the same infusion bag or administered simultaneously in the same infusion line.
- The product MUST NOT be mixed with alkaline medicinal agents or solutions, in particular 5-fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of other active ingredients. Alkaline medicinal agents or solutions will adversely affect the stability of oxaliplatin.

Instructions for use with folinic acid (e.g. with calcium folinate or disodium folinate)
250 to 500 ml of 5 % (50 mg/ml) glucose infusion solution containing 85 mg/m² oxaliplatin is infused simultaneously by the i.v. route with the folinic acid infusion solution (folinic acid in 5 % glucose) using a Y-line placed immediately before the site of infusion, over a period of 2 to 6 hours.

The 2 medicinal products must **not** be mixed in the same infusion bag. The folinic acid must not contain trometamol as a constituent, and only isotonic 5 % glucose solution may be used for its dilution. Never use any alkaline or sodium chloride solution, or any other solution containing chloride for dilution.

Instructions for use with 5-fluorouracil

Oxaliplatin should always be administered before fluoropyrimidines, i.e. 5-fluorouracil.

After the administration of Oxaliplatin medac the access must be rinsed through before the administration of 5-fluorouracil.

For further information on medicinal products given in combination with oxaliplatin, see the corresponding Summary of Product Characteristics.

Reconstituted solutions showing signs of precipitation must not be used, and should be destroyed with due observation of legal regulations for disposal of hazardous waste (see below).

Use only the recommended solvents (see below).

Only clear solutions without particles should be used.

Preparation of the infusion solution
Withdraw the required amount of concentrate from the vial(s) and then dilute with 250 ml to 500 ml of a glucose 5 % (50 mg/ml) solution to give an oxaliplatin concentration between 0.2 mg/ml and 0.7 mg/ml. The concentration range over which the physico-chemical stability of oxaliplatin has been demonstrated is 0.2 mg/ml to 2 mg/ml.

Administer by intravenous infusion.

After dilution in glucose 5 % (50 mg/ml) solution, chemical and physical in-use stability has been demonstrated for 48 hours at 2 °C to 8 °C and for 6 hours at +25 °C.

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

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

The medicinal product is for single use only. Any unused infusion solution should be discarded (see chapter “Waste disposal” below).

Never use sodium chloride or chloride containing solutions for dilution.

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

Infusion of the solution
The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 to 500 ml of a glucose 5 % (50 mg/ml) solution to give a concentration not less than 0.2 mg/ml must be infused either by peripheral vein or central venous line over 2 to 6 hours. When oxaliplatin is administered with 5-fluorouracil, the oxaliplatin infusion must precede the administration of 5-fluorouracil.

Waste disposal
Remnants of this medicinal product and all material used for dilution and administration must be destroyed in accordance with the hospital’s standard procedures for cytotoxic substances and local requirements for disposal of hazardous waste.