Package leaflet: Information for the user

Oxaliplatin Vianex 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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:
1. What Oxaliplatin Vianex is and what it is used for
2. What you need to know before you use Oxaliplatin Vianex
3. How to use Oxaliplatin Vianex
4. Possible side effects
5. How to store Oxaliplatin Vianex
6. Contents of the pack and other information

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

Oxaliplatin Vianex is used to treat metastatic (advanced) cancer of the large intestine or rectum or as additional treatment following surgery to remove a tumour in the large intestine.

Oxaliplatin Vianex is used in combination with other anticancer medicines called 5-fluorouracil (5-FU) and folinic acid (FA).

Oxaliplatin Vianes is a medicine used in the treatment of tumour diseases.

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

Do not use Oxaliplatin Vianex
- if you are allergic to oxaliplatin or any of the other ingredient of this medicine (listed in section 6);
- if you are breast-feeding;
- if you already have a reduced number of blood cells (white blood cells and/or blood platelets);
- if you already have tingling and numbness in the fingers and/or toes and have difficulties performing exacting tasks such as button up clothes;
- if you have severe kidney problems.

Warnings and precautions
Talk to your doctor or pharmacist before the administration of Oxaliplatin Vianex:
- if you ever have suffered from an allergic reaction to platinum-containing medicines such as carboplatin or cisplatin. Allergic reactions can occur during any oxaliplatin infusion;
- if you have moderate kidney problems;
- if you have liver problems;
- if you are pregnant or planning a pregnancy. It is very important that you discuss this with your doctor before you receive treatment;
- if you have low blood values after previous treatment with oxaliplatin. Your doctor will have to perform tests to investigate if you have sufficient blood values before treatment starts;
- if you have symptoms of nerve injuries such as weakness, feeling of numbness, disturbance of taste or abnormal sensations after previous treatment with oxaliplatin. These symptoms can be caused by cold. Tell your doctor if you notice any of the symptoms, particularly if they are uncomfortable and/or last more than 7 days. Your doctor will perform neurological examinations, before and during treatment, particularly if you receive other medicines, that can cause nerve injuries. Symptoms of nerve injuries may persist after end of treatment;
- if you also receive 5-fluorouracil, because of the increased risk of diarrhoea, vomiting, mouth ulcers and abnormal blood parameters.

Read the section about fertility, pregnancy and breast-feeding even if you are a man.

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

Pregnancy, breast-feeding and fertility
Oxaliplatin Vianex must not be used during pregnancy. It is important, that you tell your doctor if you are pregnant. You must tell your doctor immediately if you become pregnant during treatment.

Breast-feeding must be discontinued before treatment with Oxaliplatin Vianex starts.

Contraceptives must be used during treatment with oxaliplatin and for 4 month after end of treatment for women and 6 month after end of treatment for men.

Oxaliplatin may cause infertility, which may be permanently. Male patients are advised not to father children during and up to 6 months after treatment and to seek advice on freezing sperm before start of treatment.

Driving and using machines
Treatment with Oxaliplatin Vianex may increase the risk of dizziness, nausea and vomiting and other neurological symptoms which affect your movement and balance which may result in reduced or moderate ability to drive or use machines. Visual impairment, especially temporary decreased vision (reversible after discontinuation of the treatment) may affect your ability to drive or to use machines.

You alone are responsible to decide if you are in fit condition to drive a motor vehicle or perform other tasks that require increased alertness. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines. Information on these effects can be found in other sections. Read all the information in this leaflet for guidance. Talk to your doctor or pharmacist if you are unsure.

3. How to use Oxaliplatin Vianex

For adults only.
Oxaliplatin Vianex will be prescribed to you by a doctor specialized in cancer treatment. Oxaliplatin Vianex is given by injection into a vein (an intravenous infusion) over a 2 to 6 hour period. The dose of Oxaliplatin Vianex is based on your body surface (calculated from height and weight). The dose also depends on the results of the blood tests and whether you have previously experienced side effects with Oxaliplatin Vianex.

The recommended dose for adults including elderly is 85 mg/m\(^2\) of body surface once every two weeks.

Your doctor will decide the duration of the treatment. If you are given oxaliplatin after surgery to remove a tumor in the large intestine, the duration of treatment is no more than 6 month.

The needle must remain in the vein while the medicine is administered. If the needle comes out or becomes loose, the solution can be injected outside the vein (you may experience discomfort and pain) – **tell the doctor or nurse immediately**.

**If you are given more Oxaliplatin Vianex than you should**
As this medicine is administered in a hospital it is unlikely that you will be given too little or too much. Ask your doctor if you are concerned.

**If administration of Oxaliplatin Vianex is forgotten**
Oxiplatin must be given regularly. Be careful that you do not miss any treatment. Talk to your doctor if you miss a treatment. Your doctor will decide when you should have the next dose of oxaliplatin.

**If you stop treatment with Oxaliplatin Vianex**
Stopping treatment with oxaliplatin may lead a recurrent tumor growth. Do not stop treatment with oxaliplatin before you have been talking to your doctor.

If you have any further questions on the use of this medicine, 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 next treatment.

**Tell your doctor immediately, if you experience any of the following:**

- Symptoms of an allergic reaction such as swollen hands, feet, ankles, face, lips, mouth and throat (which may cause difficulties swallowing or breathing);
- Persistent or severe diarrhoea or vomiting;
- Sore lips or mouth ulcers;
- Abnormal bruising, bleeding or signs of infection such as sore throat and fever;
- Unexplained symptoms from the respiratory tract such as cough without mucous, difficulty in breathing or affected voice;
- Occurrence of blood or dark brown coffee-grounds in vomit.

Other known side effects of oxaliplatin:
**Very common** (affects more than 1 user in 10):
- Sensation of discomfort at the injection site during the infusion;
- Fever, trembling (tremor), mild or severe tiredness, body pain;
- Increase in weight, loss of appetite, constipation;
- Headache, back pain;
- Swelling of the nerves to your muscles, neck stiffness, abnormal tongue sensation which may alter your speech, taste disorders, stomatitis/mucositis (sore lips or mouth ulcers);
- Stomach pain;
- Abnormal bleeding including nose bleeds;
- Cough, difficulty in breathing;
- Allergic reactions, skin rash possibly red and itchy, mild hair loss (alopecia);
- Alteration in results of blood tests including abnormal liver function tests.

- Oxaliplatin Vianex may affect nerves (peripheral neuropathy). You may experience tingling and/or numbness in the fingers, toes, around the mouth or in the throat, which may sometimes occur in association with cramps. These side effects are often caused by exposure to cold e.g opening a refrigerator or holding a cold drink. You may also have difficulty in performing exacting tasks such as button up clothes. Although most of these symptoms disappear completely on their own, continued discomfort with weakness or numbness caused by nerve injuries after end of treatment is possible.

- Some people have experienced a tingling, shock-like sensation, which is radiating down the arm or body when the neck is flexed.

- Oxaliplatin Vianex can sometimes cause an unpleasant sensation in the throat, in particular when swallowing, which gives a sensation of shortness of breath. If this sensation occurs, it usually happens during or within hours of the infusion and may be caused by cold. Although unpleasant, it will not last long and goes away without the need for any treatment. Your doctor may decide to alter your treatment as a result.

- Oxaliplatin may cause diarrhoea, nausea and vomiting; medicine to prevent these symptoms is usually given to you by your doctor before treatment and may also be given after treatment.

- Oxaliplatin causes a temporary reduction in the number of blood cells. A reduction of red blood cells may cause anaemia, abnormal bleedings or bruising (due to a reduced number of blood platelets). Reduction in the number of white blood cells may increase your susceptibility to infections. Your doctor will perform blood tests to monitor that you have sufficient number of blood cells before you start treatment and before each treatment course.

**Common** (affects 1 to 10 users in 100):
- Infection caused by a reduction in the number of white blood cells;
- Indigestion and heart burn, hiccups, flush and dizziness;
- Increased sweating and affected nails, flaking skin;
- Chest pain;
- Affected lungs and runny nose;
- Joint and bone pain;
- Pain on passing urine and changes in kidney function, changes in frequency of passing urine, dehydrating;
- Blood in urine/stools, swelling of veins, blood clots in the lung;
- Depression and sleep disorders;
- Irritation of the eyes (conjunctivitis) and visual disturbances;
- Increased blood pressure;
- Gastrointestinal bleeding;
- Weight loss;
- Fever accompanied by low blood cell count.

**Uncommon** (affects 1 to 10 users in 1,000):
- Blockage or swelling of the intestine;
- Restlessness.

**Rare** (affects 1 to 10 users in 10,000):
- Impaired hearing;
- Scarring and thickening of the lung with difficulty in breathing, occasionally fatal;
- Visual impairment, inflammation of the optic nerve;
- Reversible Posterior Leukoencephalopathy Syndrome (a reversible, rapidly evolving neurological condition, which can include seizure, hypertension, headache, confusion, blindness, and other visual and neurological disturbances);
- Pancreatitis.

**Very rare** (affects less than 1 user in 10,000):
- Appearance of blood or dark brown coffee-grounds in vomit;
- Impaired liver function;
- Impaired kidney function e. g. kidney failure.

**Not known** (frequency cannot be estimated from the available data)
- Breakdown of red blood cells, reduced number of blood platelets and kidney failure (hemolytic uremic syndrome);
- Cramps.

**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 national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. **How to store Oxaliplatin Vianex**

Keep this medicine out of the sight and reach of children.
This medicine does not require any special storage conditions before opening.
Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.

Oxaliplatin should not come into contact with eyes or skin. In case of accidental spillage onto skin, seek medical advice.

When the infusion has finished, the remaining Oxaliplatin Vianex must be disposed of carefully by the doctor or nurse.

**Disposal:** Remainder of the medicinal product as well as all materials that have been used for reconstitution, for dilution and administration must be discarded according to official standard procedures applicable to cytotoxic agents.
6. Contents of the pack and other information

What Oxaliplatin Vianex contains
- The active substance is oxaliplatin.
- 1 ml reconstituted concentrated solution contains 5 mg oxaliplatin.
  50 mg vial: One vial contains 50 mg oxaliplatin for reconstitution with 10 ml solvent.
  100 mg vial: One vial contains 100 mg oxaliplatin for reconstitution with 20 ml solvent.
- The other ingredient is lactose monohydrate

What Oxaliplatin Vianex looks like and contents of the pack
White to off-white powder.

Pack sizes:
1 x 50 mg vial
1 x 100 mg vial

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:
<[To be completed nationally]>

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The following information is intended for healthcare professionals only

Instructions for handling

Oxaliplatin Vianex 5 mg/ml powder for solution for infusion
CYTOSTATIC

As with other potentially toxic compounds, caution should be exercised when handling and preparing Oxaliplatin Vianex solutions.

Instructions for handling
The handling of this cytotoxic medicinal product by health care professionals requires every precaution to protect the personnel handling the medicinal product and the surrounding environment.

The preparation of the injectable cytotoxic solution 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 according to the guidelines of the hospital. It requires a preparation area reserved for the preparation of the medicinal product. It must be forbidden to smoke, eat or drink in this area. The personnel must be provided with appropriate handling materials, especially long sleeved gowns, protection masks, caps, safety goggles, sterile single-use gloves, protective covers for the work area and collection bags for waste.
Body fluids such as vomit and faeces must be handled with care. Pregnant women should avoid handling cytotoxic agents. Broken containers must be treated with the same precautions and considered as contaminated waste. Contaminated waste must be incinerated in individually labelled rigid containers. See the section “Disposal” below.
If Oxaliplatin Vianex powder, reconstituted solution or infusion solution should come into contact with skin or mucosa, wash immediately and thoroughly with water.

**Special instructions for reconstitution and administration**
- Do not use injection material containing aluminium.
- Do not administer Oxaliplatin Vianex undiluted.
- Only glucose solution 50 mg/ml (5%) for infusion must be used as solvent. Do not reconstitute or dilute Oxaliplatin Vianex with sodium chloride solution or other chloride containing solutions.
- Oxaliplatin Vianex must not be mixed with other medicinal products in the same infusion bag or infusion tube.
- Do not mix Oxaliplatin Vianex with alkaline medicinal products or solutions, particularly 5-fluorouracil (5-FU), folinic acid (FA)-products containing trometamol as an excipient and trometamol salts of other medicinal products. Alkaline medicinal products or solutions have a negative effect on the stability of oxaliplatin.

**Instructions for use concomitantly with folinic acid (FA) (e.g. calcium folinate or sodium folinate)**
Oxaliplatin 85 mg/m² as an intra venous infusion in 250-500 ml of glucose solution 50 mg/ml (5%) can be administered concomitantly with folinic acid (FA) as an intravenous infusion in glucose solution 50 mg/ml (5%) during 2-6 hours, through a three way cock stop. Oxaplatin and folinic acid must not be combined in the same infusion bag. Medicine with folinic acid must not contain trometamol as an excipient and medicine with folinic acid must only be diluted with isotonic glucose solution 50 mg/ml (5%). Solution containing alkaline or solution containing sodium chloride or other chloride containing solutions must not be used.

**Instruction for administration concomitantly with 5-fluorouracil (5-FU)**
Oxaliplatin must always be administered before fluoropyrimidines, i.e. 5-fluorouracil (5-FU). Following administration of Oxaliplatin Vianex, the line should be flushed and thereafter 5-fluorouracil (5-FU) can be administered.

For further information on concomitant use of other medicinal products, see the respective summary of product characteristics.

- Use only the recommended solutions for dilution (see below).
- Reconstituted solutions with signs of precipitation must not be used, but destroyed in accordance with stated requirements related to the disposal of hazardous waste (see below).

**Reconstitution of solution (5 mg oxaliplatin/ml)**
For reconstitution of the solution only water for injections or glucose solution 50 mg/ml (5 %) should be used:

- Oxaliplatin Vianex 50 mg: add 10 ml of solvent to obtain a concentration of 5 mg oxaliplatin/ml.
- Oxaliplatin 100 mg: add 20 ml of solvent to obtain a concentration of 5 mg oxaliplatin/ml.

From a microbiological and chemical point of view, the reconstituted solution must be diluted immediately with glucose solution 50 mg/ml (5%).

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

The medicinal product is for single use only. Any unused solution should be destroyed.

**Dilution for infusion**

Withdraw the required amount of reconstituted solution from the vial(s) and dilute with 250-500 ml glucose solution 50 mg/ml (5%) to obtain a concentration of 0.2-0.7 mg/ml. Physical and chemical stability for oxaliplatin has been demonstrated for concentrations between 0.2 mg/ml and 2 mg/ml.

After dilution with glucose solution 50 mg/ml (5%) chemical and physical stability has been demonstrated for 24 hours at 2°C - 8°C. From a microbiological point of view the product must be used immediately.

If it is not used immediately storage times and conditions prior to and during use are the responsibility of the user. This storage time should not exceed 24 hours at 2°C - 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 only for single-use. Unused solutions must be discarded, see the section on disposal.

Sodium chloride solutions or chloride containing solutions must never be used for reconstitution or dilution.

The compatibility for oxaliplatin infusion solution has been tested with PVC-based infusion bags and infusion administration sets.

**Infusion**

Administer by intravenous infusion.

Administration of Oxaliplatin Vianex does not require prehydration.

Oxaliplatin Vianex diluted in 250-500 ml glucose solution 50 mg/ml (5%) with a oxaliplatin concentration of at least 0.2 mg/ml must be infused into a peripheral vein or central venous line during 2-6 hours. When Oxaliplatin Vianex is administered with 5-fluorouracil (5-FU), the infusion with Oxaliplatin Vianex should take place before administration of 5-fluorouracil (5-FU).

**Shelf life**

*Reconstituted solution in the original vial:*

From a microbiological and chemical point of view, the reconstituted solution should be diluted immediately with glucose solution 50 mg/ml (5%).

*Solution for infusion:*

After reconstitution with glucose solution 50 mg/ml (5%), 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 infusion preparation should be used immediately. If not used immediately following dilution 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.

**Disposal**
Remainder of the medicinal product as well as all materials that have been used for reconstitution, for dilution and administration must be discarded according to official standard procedures applicable to cytotoxic agents.