Package leaflet: Information for the user

Geneplatin 5mg/ml concentrate for solution for infusion
Oxaliplatin

Read all of this leaflet carefully before you start taking 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 Geneplatin is and what it is used for

The active ingredient of Geneplatin is oxaliplatin.

Geneplatin 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). Geneplatin is used in combination with other anticancer medicines called 5 fluorouracil and folinic acid.

Geneplatin is an antineoplastic or anticancer drug and contains platinum.

2. What you need to know before you take Geneplatin

Do not take Geneplatin
- 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

Take special care with Geneplatin

- If you have ever suffered an allergic reaction to platinum-containing medicines such as carboplatin, cisplatin. Allergic reactions can occur during any oxalipaltin infusion
- If you have moderate or mild kidney problems
- If you have any liver problems

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. Male patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 6 months.

Talk to your doctor or pharmacist before taking Geneplatin.

Other medicines and Geneplatin
Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription.

Pregnancy, breast-feeding and fertility
- It is not recommended that you become pregnant during treatment with oxaliplatin and must use an effective method of contraception. Female patients should take appropriate contraceptive measures during and after cessation of therapy continuing for 4 months. If you are pregnant, 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 get pregnant during your treatment, you must immediately inform your doctor.
- You must not breast-feed while you are treated with Oxaliplatin.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Geneplatin treatment may result in 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 Geneplatin, do not drive, operate heavy machines, or engage in dangerous activities.

3. How to take Geneplatin

Geneplatin is intended only for adults.
For single use only.

Dosage
The dose of Geneplatin is based on your body surface area. This is calculated from your height and weight.
The usual dose for adults including the elderly is 85mg/m^2 of body surface area.

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

Method and route of administration

- Geneplatin will be prescribed for you by a specialist in cancer treatment.
- You will be treated by a healthcare professional, who will have made up the required dose of Geneplatin
- Geneplatin is given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period
- Geneplatin will be given to you at the same time as folinic acid and before the infusion of 5 fluorouracil.

Frequency of administration
You should usually receive your infusion once every 2 weeks.

Duration of treatment
The duration of the treatment will be determined by your doctor.
Your treatment will last a maximum of 6 months when used after complete resection of your tumour.

If you take more Geneplatin than you should
As this medicine is administered by a healthcare professional it is highly unlikely that you will be given too much or too little.
In case of overdose, you may experience increased side effects. Your doctor will give you appropriate treatment for these side effects.

If you miss a dose of Geneplatin
If you think you have missed a dose please talk to your nurse or doctor in charge.
If you have any questions about your treatment, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, Geneplatin 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.
You will find described below the side effects that you could experience.
Tell your doctor immediately if you notice any of the following:

- Abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature.
- Persistent or severe diarrhea or vomiting.
- Presence of blood or dark brown coffee-coloured particles in your vomit.
- Stomatitis/mucositis (sore lips or mouth ulcers).
- Unexplained respiratory symptoms such as dry cough, difficulties in breathing or crackles.

Other known side effects of Geneplatin are:

Very common: may affect more than 1 in 10 people

- Geneplatin can affect your 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 effects are 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 themselves completely there is a possibility of persistent symptoms of peripheral sensory neuropathy 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.
- Geneplatin 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 goes away without the need for any treatment.
  Your doctor may decide to alter your treatment as a result.
- Geneplatin may cause diarrhea, mild nausea (feeling sick) and vomiting (being sick); however medication to prevent the sickness is usually given to you by your doctor before treatment and may be continued after treatment.
- Geneplatin causes temporary reduction in the number of blood cells. The reduction of red cells may cause anemia (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.
- Sensation of discomfort close to or at the injection site during the infusion.
- Fever, rigors (tremors), mild or severe tiredness, body pain.
- Weight changes, loss or lack of appetite, taste disorders, constipation.
- Headache, back pain.
- Swelling of the nerves to your muscles, neck stiffness, abnormal tongue sensation possibly altering speech, stomatitis/mucositis (sore lips or mouth ulcers).
- Stomach pain.
- Abnormal bleeding including nose bleeds.
- Coughing, difficulty in breathing.
- Allergic reactions, skin rash which may be red and itchy, mild hair loss (alopecia).
- Alteration in blood tests including those relating to abnormalities in liver function.

Common: may affect up to 1 in 10 people

- Infection due to a reduction in white blood cells.
- Indigestion and heart burn, hiccups, flushing, dizziness.
- Increased sweating and nail disorders, flaking skin.
- Chest pain.
- Lung disorders and runny nose.

- Joint pain and bone pain.
- Pain on passing urine and changes in kidney function, changes of frequency of urination, dehydration.
- Blood in the urine/stools, swelling of the veins, clots in the lung.
- Depression and insomnia.
- Conjunctivitis and visual problems.

Uncommon: may affect up to 1 in 100 people
- Blockage or swelling of the bowel.
- Nervousness.

Rare: may affect up to 1 in 1,000 people
- Loss of hearing
- Scarring and thickening in the lungs with difficulties in breathing, sometimes fatal (interstitial lung disease)
- Reversible short-term loss of vision.

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

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Geneplatin

Prior to mixing this medicinal product does not require any special temperature storage conditions; store in the original packaging to protect from light. Do not freeze.

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

After dilution of the concentrate for solution for infusion 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 8 hours at $\leq$ 25°C

Geneplatin should not come into contact with the eyes or skin. If there is any accidental spillage, tell the doctor or nurse immediately.
When the infusion has finished, Geneplatin will be disposed of carefully by the doctor or nurse.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Geneplatin contains:

The active substance is oxaliplatin.
Each vial contains 50 mg or 100 mg of oxaliplatin.
The other ingredient is water for injection and Nitrogen.

What Geneplatin looks like and contents of the pack

Geneplatin vials contain a concentrate for solution for infusion.
Each vial contains 50 mg or 100 mg of oxaliplatin in water for injections.
The vials are supplied in cartons of one vial.

Marketing Authorisation Holder and Manufacturer:

Genepharm S.A.
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The following information is intended for medical or healthcare professionals only:

PREPARATION GUIDE FOR USE WITH GENEPLATIN 5 MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION

It is important that you read the entire contents of this procedure prior to the preparation of the Geneplatin solution for infusion

1. FORMULATION

Geneplatin5 mg/ml concentrate for solution for infusion is a clear,
colourless liquid containing 5 mg/ml oxaliplatin in water for injections.

2. PRESENTATION

Geneplatin is supplied as single-dose vials. Each box contains one Geneplatin vial (50 mg or 100 mg).
The Geneplatin10 ml vial is a Type I clear glass of 50 mg oxaliplatin concentrate for solution for infusion with bromobutyl elastomer stopper.
The Geneplatin20 ml vial is a Type I clear glass of 100 mg oxaliplatin concentrate for solution for infusion with bromobutyl elastomer stopper.

Geneplatin as packaged for sale:
This medicinal product must be kept in the outer carton in order to be protected from light and must not be frozen.

Solution for infusion:
After dilution of the concentrate for solution for infusion 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 8 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.
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.

3. RECOMMENDATIONS FOR THE SAFE 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 healthcare 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 integrity of the product, 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 chapter "Disposal".
If oxaliplatin concentrate for solution for infusion or solution for infusion, should come into contact with skin, wash immediately and thoroughly with water.
If oxaliplatin concentrate for solution for infusion or solution for infusion, should come into contact with mucous membranes, wash immediately and thoroughly with water.

4. PREPARATION FOR THE INTRAVENOUS ADMINISTRATION

Special precautions for administration

- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only glucose 5 % (50 mg/ml) infusion solution is to be used as a diluent. DO NOT dilute for infusion with sodium chloride or chloride containing solutions.
- DO NOT mix with any other medicinal products in the same infusion bag or administer simultaneously by the same infusion line.
- DO NOT mix with alkaline medicinal products or solutions, in particular 5 fluorouracil, folinic acid preparations containing trometamol as an excipient and trometamol salts of others active substances. Alkaline medicinal products or solutions will adversely affect the stability of oxaliplatin.

Instruction for use with folinic acid (as calcium folinate or disodium folinate)

Oxaliplatin 85mg/m² intravenous infusion in 250 to 500 ml of glucose 5 % (50 mg/ml) solution is given at the same time as folinic acid intravenous infusion in glucose 5 % (50 mg/ml) solution, over 2 to 6 hours, using a Y-line placed immediately before the site of infusion.
These two medicinal products 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 glucose 5 % (50 mg/ml) 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 medicinal products combined with oxaliplatin, see the corresponding manufacturer's summary of product characteristics.

- USE ONLY the recommended solvents (see below).
- Only clear solutions without particles should be used.

4.1 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 not less than 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 2.0 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 8 hour 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 "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.

4.2 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.

4.3 Disposal

Remnants of the medicinal product as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents in accordance with local requirements related to the disposal of hazardous waste.