INFORMATION FOR THE USER

Eloxatin ®5 mg/ml

concentrate for solution for infusion

OXALIPLATIN

Read all of this leaflet carefully before you start using this medicine.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor, your pharmacist or nurse.

• If you get any side effects, talk to you 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 ELOXATIN IS AND WHAT IT IS USED FOR

The active ingredient of Eloxatin is oxaliplatin. Eloxatin 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). Eloxatin is used in combination with other anticancer medicines called 5 fluorouracil and folinic acid. Eloxatin is an antineoplastic or anticancer drug and contains platinum.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE ELOXATIN

Do not use Eloxatin if:

• You are allergic to Oxaliplatin,

• You are breast-feeding,

• You already have a reduced number of blood cells,

• You already have tingling and numbness in the fingers and/or toes, and have difficultly performing delicate tasks, such as buttoning clothes,

• You have severe kidney problems.

Warning and precautions

Talk to your doctor or pharmacist before taking Eloxatin

• If you have ever suffered an allergic reaction to platinum-containing medicines such as carboplatin, 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 heart beat, 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, and may need to potentially reduce the dose of Eloxatin, or delay or stop Eloxatin treatment.

• 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 diarrhea, tell your doctor.

• If you have sore lips or mouth ulcers (mucositis/ stomatitis), tell your doctor.

• If you have diarrhea, or a reduction in white blood cells or platelets, tell your doctor. Your doctor may reduce the dose of Eloxatin or postpone your treatment with Eloxatin.

• If you have unexplained respiratory symptoms such as cough, or any difficulties in breathing, tell your doctor. Your doctor may stop your treatment with Eloxatin.

• 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 Eloxatin, 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 redbrown 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 “coffeegrounds”, 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 Eloxatin

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

Pregnancy , breast-feeding and fertility

Pregnancy

• 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 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.

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

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

Driving and using machines

Oxaliplatin 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 Eloxatin, do not drive, operate heavy machines or engage in dangerous activities.

3. HOW TO USE ELOXATIN

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

Dosage

The dose of Eloxatin is based on your body surface area. This is calculated from your height and weight. The usual dose for adults including the elderly is 85 mg/m2 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 Eloxatin.

Method and route of administration

• Eloxatin 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 Eloxatin.

• Eloxatin is given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period.

• Eloxatin 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 use more Eloxatin 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 may give you appropriate treatment for these side effects. If you have any questions about your treatment, ask your doctor, nurse 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 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

• 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 bruising, bleeding, or signs of infection such as a sore throat and high temperature,

• Persistent or severe diarrhoea or vomiting,

• Presence of blood or dark brown coffee coloured particles in your vomit,

• Stomatitis/mucositis (sore lips or mouth ulcers),

• Respiratory symptoms such as dry or wet cough, difficulties in breathing or crackles, shortness of breath and wheezing as these may be indications of a serious lung disease that may lead to death,

•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).

• Stroke symptoms (including sudden severe headache, confusion, trouble seeing in one or both eyes, numbness or weakness of face, arm or leg usually on one side, face dropping, trouble walking, dizziness loss of balance and speech difficulty),

• 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).

Other known side effects of Eloxatin are:

Very common (may affect more than 1 in 10 people)

• Eloxatin 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 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.

• Eloxatin 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.

• Eloxatin may cause diarrhoea, 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.

• Eloxatin 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.

• 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,

• Serious infection of the blood in addition to a reduction in white blood cells (neutropenic sepsis), which may be fatal,

• Reduction in white blood cells accompanied by fever > 38.3°C or a prolonged fever > 38°C for more than one hour (febrile neutropenia),

• 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,

• High blood pressure,

• Depression and insomnia,

• Conjunctivitis and visual problems,

• Decreased levels of calcium in the blood,

• Fall.

Uncommon (may affect up to 1 in 100 people)

• Serious infection of the blood (sepsis), which may be fatal,

• 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.

• 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)

• Presence of blood or dark brown coffee coloured particles in your vomit.

• Kidney disease where you pass little or no urine (symptoms of acute renal failure)

• Vascular disorders of liver.

Frequency not known (frequency cannot be estimated from the available data)

• Allergic vasculitis (inflammation of blood vessels),

• Auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia), pancytopenia,

• Serious infection of the blood and low blood pressure (septic shock), which may be fatal,

• Convulsion (uncontrolled shaking of the body),

• Spasm of the throat causing difficulty in breathing,

• Extreme tiredness with decreased number of red blood cells, and shortness of breath (haemolytic anaemia), alone or combined with low platelet count and kidney disease where you pass little or no urine (symptoms of Haemolytic-uraemic syndrome), which may be fatal, have been reported.

• 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),

• Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal,

• Oesophageal inflammation (inflammation of the lining of the esophagus - the tube that connects your mouth with your stomach resulting in pain and swallowing difficulty),

• Abdominal pain, nausea, bloody vomit or vomit that looks like „coffee grounds", or darkcolored/tarry stools (symptoms of gastrointestinal ulcer, with potential bleeding or perforation), which may be fatal,

• Decreased blood flow to the intestine/bowel (intestinal ischaemia), which may be fatal,

• Risk of new cancers. Leukaemia, a form of blood cancer, has been reported in patients after taking Eloxatin in combination with certain other medicines. Talk to your doctor about the potential for increased risk of this type of cancer when taking Eloxatin and certain other medicines.

•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 HPRA Pharmacovigilance,

Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Eloxatin

• Keep this medicine out of the sight and reach of children.

• Prior to mixing this medicine must be kept in the outer carton in order to be protected from light and must not be frozen.

• Do not use this medicine after the expiry date which is stated on the outer pack and vial label. The expiry date refers to the last day of the month.

Eloxatin 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, Eloxatin will be disposed of carefully by the doctor or nurse.

6. Contents of the pack and other information

What ELOXATIN contains

The active substance is called oxaliplatin. Each vial contains 50 mg, 100 mg or 200 mg of oxaliplatin. The other ingredient is water for injections.

What ELOXATIN looks like and contents of the pack

ELOXATIN vials contain a concentrate for solution for infusion. Each vial contains 50 mg, 100 mg or 200 mg oxaliplatin in water for injections.

The vials are supplied in cartons of one vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Sanofi-aventis Ireland Ltd. T/A SANOFI,

Citywest Business Campus,

Dublin 24

Manufacturer

Sanofi-Aventis Deutschland GmbH

Industriepark Höchst

65926 Frankfurt am Main

Germany

This medicinal product is authorised in

the Member States of the EEA under the

following names:

France: OXALIPLATINE WINTHROP 5 mg/ml, solution à diluer pour perfusion

Germany: Oxaliplatin Winthrop 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung

Greece: Eloxatin

Ireland: Eloxatin 5 mg/ml concentrate for solution for infusion

Portugal: Eloxatin 5 mg/ml, concentrado para solução para perfusão

Slovenia: Eloxatin 5mg/ml koncentrat za raztopino za infundiranje

This leaflet was last revised in: November 2022

The following information is intended for medical or healthcare professionals only

PREPARATION GUIDE FOR THE USE WITH

Eloxatin ®5 mg/ml concentration for solution for infusion

OXALIPLATIN

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

1. FORMULATION

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

2. PRESENTATION

ELOXATIN is supplied as single-dose vials. Each box contains one ELOXATIN vial (50 mg, 100 mg or 100 mg).

The ELOXATIN 10 ml vial is a Type I clear glass of 50 mg oxaliplatin concentrate for solution for infusion with bromobutyl elastomer stopper.

The ELOXATIN 20 ml vial is a Type I clear glass of 100 mg oxaliplatin concentrate for solution for infusion with bromobutyl elastomer stopper.

The ELOXATIN 40 ml vial is a Type I clear glass of 200 mg oxaliplatin concentrate for solution for infusion with bromobutyl elastomer stopper.

ELOXATIN 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 24 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 24 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 "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.