

## **Package leaflet: Information for the user**

### **Oxaliplatin 5 mg/ml concentrate for solution for infusion**

oxaliplatin

**Read all of this leaflet carefully before being 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.
- 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 5 mg/ml concentrate for solution for infusion is and what it is used for
2. What you need to know before being given Oxaliplatin 5 mg/ml concentrate for solution for infusion
3. How Oxaliplatin 5 mg/ml concentrate for solution for infusion is given
4. Possible side effects
5. How to store Oxaliplatin 5 mg/ml concentrate for solution for infusion
6. Contents of the pack and other information

#### **1. What Oxaliplatin 5 mg/ml concentrate for solution for infusion is and what it is used for**

This medicine contains the active substance oxaliplatin. Oxaliplatin 5 mg/ml concentrate for solution for infusion is an antineoplastic or anticancer drug and contains platinum.

Oxaliplatin 5 mg/ml concentrate for solution for infusion 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 is used in combination with other anticancer medicines called 5-fluorouracil and folinic acid.

#### **2. What you need to know before being given Oxaliplatin 5 mg/ml concentrate for solution for infusion**

**You must not be given Oxaliplatin 5 mg/ml concentrate for solution for infusion if you:**

- are allergic to oxaliplatin
- already have a reduced number of blood cells
- already have tingling and numbness in the fingers and/or toes, and have difficulty performing delicate tasks, such as buttoning clothes
- have severe kidney problems.

You must not breast-feed whilst you are treated with oxaliplatin.

### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before being given Oxaliplatin 5 mg/ml concentrate for solution for infusion:

- if you have ever suffered an allergic reaction to platinum-containing medicines such as 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.

Consult your doctor if one of the above warnings applies to you or has done in the past.

### **Other medicines and Oxaliplatin 5 mg/ml concentrate for solution for infusion**

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 you must use an effective method of contraception. Female patients should take appropriate contraceptive measures during and after stopping 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 being given any treatment**.

If you get pregnant during your treatment, you must immediately inform your doctor.

#### Breast-feeding

You must not breast-feed whilst 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 should take appropriate contraceptive measures during this time.

### **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 whilst being given Oxaliplatin 5 mg/ml concentrate for solution for infusion, do not drive, operate heavy machines or engage in dangerous activities.

### **3. How Oxaliplatin 5 mg/ml concentrate for solution for infusion is given**

Oxaliplatin 5 mg/ml concentrate for solution for infusion is intended for adults only.  
For single use only.

#### **Dosage**

The dose of oxaliplatin 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/m<sup>2</sup> 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 oxaliplatin.

#### **Method and route of administration**

- Oxaliplatin 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 oxaliplatin.
- Oxaliplatin is given by slow injection into one of your veins (an intravenous infusion) over a 2 to 6 hour period.
- Oxaliplatin 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 are given more Oxaliplatin 5 mg/ml concentrate for solution for infusion 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 further questions about 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.

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), Abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature. Your doctor will take blood to check that you have sufficient blood cells before you start treatment and before each subsequent course
- Persistent or severe diarrhoea or vomiting. Inflammation of the large bowel which may cause abdominal pain or diarrhoea possibly with blood.
- Presence of blood or dark brown coffee-coloured granules in your vomit or stools
- Sore lips or mouth ulcers (stomatitis/mucositis)
- Lung problems with difficulties in breathing (pulmonary fibrosis)
- Unexplained respiratory symptoms such as dry cough, difficulties in breathing or crackles, which is sometimes fatal (interstitial lung disease)
- 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)
- Serious infection of the blood (sepsis) in addition to a reduction in white blood cells (neutropenic sepsis) or low blood pressure (septic shock), which may be fatal
- Problems with your liver which may cause stomach pain and swelling, weight gain
- Inflammation of the pancreas with severe upper stomach pain, often with nausea and vomiting
- Blood clot in the lungs which causes chest pain and breathlessness
- Inflammation of the optic nerve causing blurred vision
- Fits (convulsions).

## Other side effects:

**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 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.

- 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 goes away without the need for any treatment.

Your doctor may decide to alter your treatment as a result.

- Rigors (tremors), mild or severe tiredness or lack of energy, body pain
- Weight increase, loss or lack of appetite, taste disorders, constipation
- Headache, back pain
- Stomach pain
- Nose bleeds
- Coughing, shortness of breath
- Skin problems
- Mild hair loss (alopecia)
- Alteration in blood tests including those relating to abnormalities in liver function
- Excessive levels of glucose (sugar) in your blood 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;
- High blood levels of sodium due to water loss from your body which can cause thirst, lethargy, weakness, irritability, muscle problems and swelling of different parts of your body
- Blood tests which show increase in lactate dehydrogenase (enzyme).
- Pain or redness close to or at the injection site during the infusion which can lead to tissue death in the case of leaking of medicine outside the vein

**Common** (may affect up to 1 in 10 people)

- Nervous symptoms including involuntary contractions of the muscles or jaw, sensation of compression of the throat or chest, or difficulty walking or moving and balance
- Symptoms which show changes in the way the cranial nerve is working such as eye and sight problems, speech and voice problems, strong facial pain
- Indigestion and heartburn, hiccups, flushing, dizziness
- Increased sweating and nail disorders, flaking skin
- Nose and throat infection and runny nose
- Neck stiffness, intolerance/dislike of bright light and headache
- Joint pain and bone pain
- Pain on passing urine and decrease in kidney function, changes of frequency of urination, dehydration
- Blood in the urine
- High blood pressure
- Depression and insomnia
- Conjunctivitis and visual problems
- Loss of weight
- Blood clot, usually in a leg, which causes pain, swelling or redness.

**Uncommon** (may affect up to 1 in 100 people)

- Condition with abnormal blood tests results which show an increase in acidity due to kidney problems (metabolic acidosis)
- Nervousness.
- Damage to the ear which may cause hearing problem (ototoxicity)
- Blockage or swelling of the bowel

**Rare** (may affect up to 1 in 1,000 people)

- Slurred speech
- Loss of hearing
- Reversible short-term loss of vision.

**Very rare (may affect up to 1 in 10,000 people)**

- Kidney disease where you pass little or no urine

**Not known** (frequency cannot be estimated from the available data)

- Spasm of the throat causing difficulty in breathing.
- Allergic vasculitis (inflammation of blood vessels)
- Auto-immune reaction leading to reduction of all blood cell lines (autoimmune pancytopenia).

### **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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie). By reporting side effects you can help provide more information on the safety of this medicine.

### **5. How to store Oxaliplatin 5 mg/ml concentrate for solution for infusion**

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

Do not use this medicine if you notice visible signs of deterioration such as particulate matter or discolouration.

This medicine does not require any special storage conditions. Do not refrigerate or freeze. Storage conditions for the diluted solutions are given in the information intended for medical and healthcare professionals.

Oxaliplatin 5 mg/ml concentrate for solution for infusion should not come into contact with the eyes or skin. If there is any accidental spillage, tell the doctor or nurse immediately.

### **6. Contents of the pack and other information**

#### **What Oxaliplatin 5 mg/ml concentrate for solution for infusion contains**

The active substance is oxaliplatin.

The other ingredient is water for injections.

#### **What Oxaliplatin 5 mg/ml concentrate for solution for infusion looks like and contents of the pack**

Oxaliplatin 5 mg/ml concentrate for solution for infusion is a concentrate for solution for infusion (a concentrated solution which is diluted to make a solution which can be given as a slow infusion via a drip).

It is a clear, colourless solution free from visible particles contained in glass containers called vials with bromobutyl stopper and flip off aluminium seal.

Each ml concentrate for solution for infusion contains 5 mg of oxaliplatin.

The 10 ml vial contains 50 mg of oxaliplatin (with a grey flip off aluminium seal).

The 20 ml vial contains 100 mg of oxaliplatin (with a red flip off aluminium seal).

The 40 ml vial contains 200 mg of oxaliplatin (with a grey flip off aluminium seal).

The vials are supplied in cartons each containing one vial.

Not all pack sizes may be marketed.

Oxaliplatin 5 mg/ml concentrate for solution for infusion has to be diluted before it can be injected into a vein.

### **Marketing Authorisation Holder and Manufacturer**

#### *Marketing authorisation holder*

Generics [UK] Limited  
Station close, Potters Bar,  
Hertfordshire EN6 1TL  
United Kingdom

#### *Manufacturer*

Strides Arcolab Polska Sp.z.o.o.  
10, Daniszewska Str  
03-230 Warsaw  
Poland

### **This medicine is authorised in the Member States of the EEA under the following names**

For NL/H/1977

The Netherlands	Oxaliplatine Mylan 5 mg/ml, concentraat voor oplossing voor infusie
Austria	Oxaliplatin Mylan 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Oxaliplatine Mylan 5 mg/ml concentraat voor oplossing voor infusie
Bulgaria	Oxaliplatin Mylan 5 mg/ml concentrate for solution for infusion
Cyprus	Oxaliplatin Mylan 5 mg/ml concentrate for solution for infusion
Czech Republic	Oxaliplatin Generics 5 mg/ml koncentrát pro infuzníroztok
Germany	Oxaliplatin Mylan 5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Denmark	Oxaliplatin Mylan 5 mg/ml koncentrat till infusionsvaeske, opløsning
Estonia	Oxaliplatin Mylan
Greece	Oxaliplatin/Mylan Concentrate Solution for Infusion 5 mg / mL
Spain	Oxaliplatino Mylan 5 mg/ml concentrado para solución para perfusión EFG
Finland	Oxaliplatin 5 mg/ml infuusiokonsentraatti, liuosta varten
France	Oxaliplatine Mylan 5 mg/ml, solution à diluer pour perfusion
Hungary	Oxaliplatin Mylan Pharma 5 mg/ml koncentrátum oldatos infúzióhoz
Ireland	Oxaliplatin 5 mg/ml concentrate for solution for infusion
Iceland	Oxaliplatin 5 mg/ml innrennslisþykkni, lausn
Italy	Oxaliplatino Mylan Pharma
Latvia	Oxaliplatin Mylan 5 mg/ml concentrate for solution for infusion
Lithuania	Oxaliplatin Mylan 5 mg/ml koncentratas infuziniam tirpalui
Luxemburg	Oxaliplatine Mylan 5 mg/ml solution à diluer pour perfusion
Malta	Oxaliplatin Mylan 5 mg/ml koncentrat għal soluzzjoni għall-infuzjoni
Norway	Oxaliplatin 5 mg/ml konsentrat til infusjonsvæske, oppløsning
Poland	Oxaliplatin Mylan, 5 mg/ml, koncentrat do sporządzania roztworu do infuzji
Portugal	Oxaliplatina Mylan

Romania	Oxaliplatină Mylan 5 mg/ml concentrat pentru soluție perfuzabilă
Sweden	Oxaplamyl 5 mg/ml koncentrat till infusionsvätska, lösning
Slovak Republic	Oxaliplatina Generics 5 mg/ml infúzny koncentrát
Slovenia	Oksaliplatin Mylan 5 mg/ml koncentrat za raztopino za infundiranje
UK	Oxaliplatin 5 mg/ml concentrate for solution for infusion

**This leaflet was last revised in**  
Dec 2016

<----->

**The following information is intended for medical or 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 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 medicinal 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 or solution for infusion, should come into contact with skin or mucous membranes, wash immediately and thoroughly with water.

## **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 drugs or solutions, in particular 5-fluorouracil (5-FU), folic acid (FA) preparations containing trometamol as an excipient and trometamol salts of others active substances. Alkaline drugs or solutions will adversely affect the stability of oxaliplatin.

### Instruction for use with folic acid (FA) (as calcium folinate or disodium folinate)

Oxaliplatin 85 mg/m<sup>2</sup> intravenous infusion in 250 ml to 500 ml of glucose 5 % (50 mg/ml) solution is given at the same time as folic acid (FA) 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. Folic 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 (5-FU). After oxaliplatin administration, flush the line and then administer 5-fluorouracil (5-FU).

### Dilution for intravenous infusion

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 obtain an oxaliplatin concentration between 0.20 mg/ml and 0.70 mg/ml. The concentration range over which the physico-chemical stability of oxaliplatin has been demonstrated is 0.20 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 2-8 °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 to 8 °C unless dilution has taken place in controlled and validated aseptic conditions.

Inspect the solution 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.

#### Infusion

The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 ml to 500 ml of a glucose 5 % (50 mg/ml) solution to give a concentration not less than 0.20 mg/ml must be infused via a central venous line or a peripheral vein over 2 to 6 hours. When oxaliplatin is administered with 5-fluorouracil (5-FU), the oxaliplatin infusion must precede the administration of 5-fluorouracil (5-FU).

#### 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.