PACKAGE LEAFLET: INFORMATION FOR THE USER

OXALIPLATIN 5 MG/ML POWDER FOR SOLUTION FOR INFUSION

(OXALIPLATIN)

Read all of this leaflet carefully before you are given Oxaliplatin.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT OXALIPLATIN IS AND WHAT IT IS USED FOR

Oxaliplatin 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 (5- FU) and leucovorin (folinic acid).

Oxaliplatin is an antineoplastic or anticancer drug and contains platinum.

2. BEFORE YOU ARE GIVEN OXALIPLATIN

You should not be given Oxaliplatin if you:

- have a known allergy to oxaliplatin or any of the excipients of Oxaliplatin.
- are breast-feeding.
- already have a reduced number of red or white 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.

Take special care with Oxaliplatin:

- 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.

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.

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

Taking other medicines:
Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicines including medicines obtained without a prescription.

Pregnancy and breast-feeding:
It is not recommended that you become pregnant during treatment with oxaliplatin. During treatment an effective method of contraception must be used. Female patients should take appropriate contraceptive measures during and after cessation of therapy, continuing 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.

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

3. HOW OXALIPLATIN IS GIVEN

Oxaliplatin 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 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 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 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 than you should:
As this medicine is administered by a healthcare professional, it is unlikely that you will be given too little or too much.
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, Oxaliplatin can cause side effects, although not everyone gets them.

Side effects may be

very common: affects more than 1 user in 10
common: affects 1 to 10 users in 100
uncommon: affects 1 to 10 users in 1,000
rare: affects 1 to 10 users in 10,000
very rare: affects less than 1 user in 10,000
not known: frequency cannot be estimated from the available data

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 diarrhoea or vomiting

- Presence of blood or dark brown coffee-coloured granules in your vomit
- Stomatitis/mucositis (sore lips or mouth ulcers)
- Unexplained respiratory symptoms such as dry cough, difficulties in breathing or crackles
- 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).

Other known side effects of oxaliplatin are:

Very common (affects more than 1 person in 10)

- 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.

- Oxaliplatin 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.
- 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.

- 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 (affects 1 to 10 users in 100)
- 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
- High blood pressure
- Depression and insomnia
- Conjunctivitis and visual problems

Uncommon (affects 1 to 10 users in 1000)
- Blockage or swelling of the bowel
- Nervousness

Rare (affects 1 to 10 users in 10000)
- 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 (affects less than 1 user in 10 000)
- Presence of blood or dark brown coffee-coloured particles in your vomit

Frequency unknown (cannot be assessed)
- Convulsion.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE OXALIPLATIN

Keep out of the reach and sight of children.

Expiry Date
Do not use Oxaliplatin after the expiry date which is stated on the vial and carton after EXP (abbreviation used for expiry date). The expiry date refers to the last day of that month.

Storing your medicine
This medicinal product does not require any special storage conditions.
Storage conditions for the diluted solutions are given in the information intended for medical and healthcare professionals.

6. FURTHER INFORMATION

What Oxaliplatin contains
The active substance of Oxaliplatin contains is oxaliplatin. The other ingredient is lactose monohydrate.

What Oxaliplatin contains looks like and contents of the pack
Each vial contains a white, lyophilised powder or plug for solution for infusion containing 50 mg or 100 mg oxaliplatin with lactose monohydrate.
The vials are supplied in cartons each containing one vial.
Oxaliplatin has to be dissolved and further diluted before it can be injected into a vein. The reconstituted and diluted solution is a clear colourless solution free from particulate matter.

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

Marketing authorisation holder and manufacturer

Marketing authorisation holder
Generics [UK] Limited t/a Mylan
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 Member States of the EEA under the following names

The Netherlands	Oxaliplatin Mylan 5 mg/ml poeder voor oplossing voor infusie
Austria	Oxaliplatin Mylan 5 mg/ml Pulver zur Herstellung einer Infusionslösung
Belgium	Oxaliplatine Mylan 5 mg/ml poeder voor oplossing voor infusie
Bulgaria	Oxaliplatin Mylan 5 mg/ml Прах за инфузионен разтвор
Cyprus	Oxaliplatin Mylan 5 mg/ml Κόνις για διάλυμα προς έγχυση
Czech Republic	Oxaliplatina Generics 5 mg/ml prášek pro připravu infuzniho roztokuGermany
	Oxaliplatin Mylan 5 mg/ml Pulver zur Herstellung einer Infusionslösung
Denmark	Oxaliplatin Mylan

Estonia	Oxaliplatin Mylan
Greece	Oxaliplatin/Mylan 5 mg/ml Κόνις για διάλυμα προς έγχυση
Spain	Oxaliplatino Mylan 5 mg/ml polvo para solución para perfusión
Finland	Oxaliplatin Mylan 5 mg/ml Infuusiokuiva-aine, liuosta varten
France	Oxaliplatine Mylan Pharma 5 mg/ml Poudre pour solution pour perfusion
Hungary	Oxaliplatin Generics (UK) 5 mg/ml por oldatos infúzióhoz
Ireland	Oxaliplatin 5 mg/ml powder for solution for infusion
Iceland	Oxaliplatin Mylan 5 mg/ml Innrennslisstofn, lausn
Italy	Oxaliplatino Mylan 5 mg/ml polvere per soluzione per infusione
Latvia	Oxaliplatin Mylan 5 mg/ml pulveris infūziju šķīduma pagatavošanai
Lithuania	Oxaliplatin Mylan 5 mg/ml milteliai infuziniam tirpalui
Luxembourg	Oxaliplatine Mylan 5 mg/ml Poudre pour solution pour perfusion
Malta	Oxaliplatin Mylan 5 mg/ml Trab għal soluzzjoni għall-infużjoni
Norway	Oxaliplatin Mylan 5 mg/ml pulver til infusjonsvæske, oppløsning
Poland	Oxaliplatin Mylan
Portugal	Nitaldrane
Romania	Oxaliplatină Mylan 5 mg/ml pulbere pentru soluţie perfuzabilă
Sweden	Oxaliplatin Mylan 5 mg/ml pulver till infusionsvätska, lösning
Slovak Republic	Oxaliplatina Generics 5 mg/ml prášok na infúzny roztok
Slovenia	Oksaliplatin Mylan5 mg/ml prašek za raztopino za infundiranje
UK	Oxaliplatin 5 mg/ml Powder for solution for infusion

This leaflet was last approved in 07/2015

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 powder, reconstituted solution 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 reconstitute or 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 (5FU), folinic 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 folinic acid (FA) (as calcium folinate or disodium folinate)
Oxaliplatin 85 mg/m² intravenous infusion in 250 ml to 500 ml of glucose 5% (50 mg/ml) solution is given at the same time as folinic 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. 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 (5FU). After oxaliplatin administration, flush the line and then administer 5-fluorouracil (5FU).

A reconstituted solution which shows signs of precipitation may not be used and should be destroyed.

Reconstitution of the solution
- To reconstitute the solution, water for injection or 5 % (50 mg/ml) glucose solution should be used.
- When using a 50 mg vial: add 10 ml solvent to obtain a solution of 5 mg oxaliplatin per ml.
- When using a 100 mg vial: add 20 ml solvent to obtain a solution of 5 mg oxaliplatin per ml.

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

The reconstituted solution is for single use only and should, from a microbiological point of view, be used immediately.
If not diluted 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 reconstitution has taken place in controlled and validated aseptic conditions.

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.

The diluted solution is a clear colourless solution free from particulate matter.

Administer by intravenous infusion.

After dilution of the reconstituted solution in glucose 5% (50 mg/ml) solution, chemical and physical in-use stability has been demonstrated for 24 hours at 2-8°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 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 (5FU), the oxaliplatin infusion must precede the administration of 5-fluorouracil (5FU).

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.