Package leaflet:
Information for the user

Oxaliplatin Hospira 5 mg/ml concentrate for solution for infusion

Oxaliplatin

Read all of this leaflet carefully before you start taking this medicine. 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 Hospira is and what it is used for
2. What you need to know before you use Oxaliplatin Hospira
3. How to use Oxaliplatin Hospira
4. Possible side effects
5. How to store Oxaliplatin Hospira
6. Contents of the pack and other information

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

The active ingredient of Oxaliplatin Hospira is oxaliplatin.

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 and folinic acid.

Oxaliplatin is an antineoplastic or anticancer drug and contains platinum.

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

Do not use Oxaliplatin Hospira if
- You are allergic to oxaliplatin or any of the other ingredients of this medicine (listed in section 6),
- 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 difficulty performing delicate tasks, such as buttoning clothes,
- You have severe kidney problems.

Warnings and precautions
Talk to your doctor or pharmacist or nurse before taking Oxaliplatin Hospira:
- If you have ever suffered an allergic reaction to platinum-containing medicines

such as carboplatin, cisplatin. Allergic reactions can occur during oxaliplatin infusion,
- If you have moderate or mild kidney problems,
- If you have any liver problems or abnormal liver function 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.

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

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 oxaliplatin, do not drive, use heavy machines or engage in dangerous activities.

Oxaliplatin Hospira contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How to use Oxaliplatin Hospira

For adults only.

Oxaliplatin is intended only for adults.

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/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 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 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 Hospira 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,
- If you faint (lose consciousness) or have an irregular heartbeat while taking Oxaliplatin Hospira, 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 red brown urine, tell your doctor. These could be signs of muscle damage (rhabdomyolysis) and could lead to kidney problems or other complications,
- 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 oxaliplatin are:

<u>Very common (may affect more than 1 in 10 people):</u>
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 (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 people):

- 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.

Not known (frequency cannot be estimated from 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,
- Heart attack (myocardial infarction), pain or uncomfortable feeling in the chest (angina pectoris),
- Inflammation of the lining of the oesophagus – the tube that connects your mouth with your stomach – resulting in pain and swallowing difficulty (oesophageal inflammation),
- Muscle pain and swelling, in combination with weakness, fever, or red-brown urine (symptoms of muscle damage called rhabdomyolysis), which may be fatal,
- Abdominal pain, nausea, bloody vomit or vomit that looks like "coffee grounds", or dark coloured/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 Oxaliplatin in combination with certain other medicines. Talk to your doctor about the potential for increased risk of this type of cancer when taking Oxaliplatin 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.

5. How to store Oxaliplatin Hospira

Please refer to the outer carton for storage condition.

Keep this medicine out of the sight and reach of children. Keep the vial in the outer carton in order to protect from light. Do not freeze.

Do not use this medicine after the expiry date which is stated on the carton.

Once diluted the infusion preparation should be used immediately. Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C and 6 hours at 25°C. If not used immediately, in-use storage times and conditions are the responsibility of the user and would not normally be longer than 24 hours at 2°C to 8°C.

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

6. Contents of the pack and other information

What Oxaliplatin Hospira contains
- The active substance is oxaliplatin.
  One ml of concentrate for solution for infusion contains 5 mg oxaliplatin.
  10 ml of concentrate for solution for infusion contains 50 mg of oxaliplatin.
  20 ml of concentrate for solution for infusion contains 100 mg of oxaliplatin.
- The other ingredients are tartaric acid, sodium hydroxide and water for injections

What Oxaliplatin Hospira looks like and contents of the pack
Oxaliplatin Hospira is in the form of a concentrate solution for infusion (a concentrated solution which is diluted to make a solution which can be given as a slow infusion via a drip). Each millilitre (ml) of solution contains 5 milligrams (mg) of oxaliplatin. It is a clear, colourless solution contained in glass containers called vials, containing 50 mg (10 ml) and 100 mg (20 ml) of oxaliplatin. The vials are wrapped in a protective plastic to reduce the risk of spillage if the vials break - these are referred to as ONCO-TAIN®. The vials are available in single packs.

The solution is then diluted in glucose 5% solution and can be given as an infusion via a drip.

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 preparations 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 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.

Special precautions for administration

- DO NOT use injection equipment containing aluminium.
- DO NOT administer undiluted.
- Only glucose 5% 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 other active substances.
- Alkaline medicinal products 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/m^2 intravenous infusion in 250 to 500 ml of glucose 5% solution is given at the same time as folinic acid (FA) intravenous infusion in glucose 5% 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 (FA) must not contain trometamol as an excipient and must only be diluted using isotonic glucose 5% solution, never in alkaline solutions or sodium chloride or chloride containing solutions.

Instruction for use with 5-fluorouracil (5-FU)
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).

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).
- Any concentrate that shows evidence of precipitation should not be used and should be destroyed with due regard to legal requirements for disposal of hazardous waste (see below).

Concentrate for solution for infusion
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.

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% solution to give an oxaliplatin concentration between 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 1.3 mg/ml.

Administer by intravenous infusion.

After dilution in glucose 5% solution, chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C and for 6 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 on "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 of the solution
The administration of oxaliplatin does not require prehydration.

Oxaliplatin diluted in 250 to 500 ml of a glucose 5% 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.

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.

October 2021
Hong Kong