Package leaflet: Information for the user

Cisplatin 1mg/ml Concentrate for Solution for Infusion
cisplatin

The name of your medicine is 'Cisplatin 1 mg/ml Concentrate for Solution for Infusion' but in the rest of the leaflet it will be called "Cisplatin Injection".

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have 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 Cisplatin Injection is and what it is used for

Cisplatin Injection contains the active substance cisplatin which forms part of a group of medicines called cytostatics, which are used in the treatment of cancer. Cisplatin can be used alone but more commonly cisplatin is used in combination with other cytostatics.

Cisplatin can destroy cells in your body that may cause certain types of cancer (tumour of testis, tumour of ovary, tumour of the bladder, head and neck epithelial tumour, lung cancer and for cervical cancer in combination with radiotherapy).

Your doctor will be able to provide you with more information.

You must talk to a doctor if you do not feel better or if you feel worse.

2. What you need to know before you use Cisplatin Injection

Do not use Cisplatin Injection:
- if you are allergic to cisplatin, similar anti-cancer medicines, other platinum containing compounds or any of the other ingredients of this medicine (listed in section 6)
- if you have very low numbers of blood cells (called 'myelosuppression'), (your doctor will check this with a blood test)
- if you are breast-feeding
- if you have severe kidney disease
- if you have hearing difficulties
- if you are dehydrated
- if you need to have a vaccine for "yellow fever"

Tell your doctor if the above applies to you before this medicine is used.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Cisplatin Injection:

- if you have any symptoms of nerve damage (peripheral neuropathy) such as pins and needles, numbness or poor sense of touch. You will be examined regularly for these symptoms and treatment may be stopped if necessary.
- if you have had radiation therapy to your head

Your doctor will carry out tests in order to determine the levels of calcium, sodium, potassium and magnesium in your blood, as well as to check your blood picture and your liver and kidney functionality and neurological function.

Cisplatin can affect bone marrow causing changes to blood cell production in the body, tell your doctor if you have unusual bleeding or bruising. Do not take aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or other medications without telling your doctor. Your doctor will test your blood frequently and check for signs of infection.

Cisplatin may cause hearing problems (ototoxicity) and kidney problems (nephrotoxicity). Renal function and hearing will be monitored prior to and during treatment.
If you experience hearing changes, you must tell your doctor.

Tell your doctor if you intend to have a vaccine during treatment with Cisplatin, some live vaccines should be avoided as they can cause serious infections, and your response to other vaccine types (inactivated) may be reduced.

Other medicines and Cisplatin Injection
Talk to your doctor,pharmacist or nurse if you are using, have recently used or might use any other medicine, for example:

- some antibiotics, such as cephalosporins, aminoglycosides and amphotericin B and some substances used in medical imaging may make the side effects of cisplatin worse; particularly kidney problems
- some water tablets called loop diuretics, antibiotics called aminoglycosides and an anti-cancer medicine called ifosfamide may make the hearing loss side effect of cisplatin worse
- bleomycin (anti-cancer medicine), methotrexate (used to treat cancer or arthritis) and paclitaxel (anti-cancer medicine) may produce more side effects if cisplatin is also being used
- cisplatin may reduce the effectiveness of anticonvulsants (used to treat epilepsy), phenytoin blood levels may need to be checked
- the effectiveness of oral anticoagulants (e.g. warfarin) may be affected, your doctor will monitor with blood tests
- buclizine, cyclizine and meclozone (antihistamine medicines), loxapine, phenothiazines and thioxanthenes (medicines used to treat psychiatric disorders) or trimethobenzamines (medicines used to prevent nausea and vomiting) may hide the symptoms of balance changes (such as dizziness or tinnitus)
- cisplatin may make the side effects of the anti-cancer medicine ifosfamide worse
- pyroxidine (vitamin B6) and altretamine (anti-cancer medicine) used in combination with cisplatin for the treatment of advanced ovarian cancer may reduce the time spent in recovery. Your doctor will discuss this with you
- bleomycin and etoposide (anti-cancer medicines) used in combination with cisplatin and lithium (used to treat mental illness) may reduce the levels of lithium in the blood. It is recommended to monitor the lithium values
- Yellow fever vaccine must not be used at the same time as treatment with cisplatin due to the risk of death resulting from the vaccination. It is recommended to use an inactive vaccine
- antigout medicines such as allopurinol, colchicine, probenecid or sulfinpyrazone reduce the levels of uric acid in the blood. Your doctor may need to change your dose of Cisplatin Injection.

Pregnancy, breast-feeding and fertility
Pregnancy
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Due to the possible risk of birth defects, male and female patients should take contraceptive measures both during treatment with cisplatin and for at least six months after treatment has ended.

Cisplatin must not be used during pregnancy unless clearly indicated by your doctor.

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

Breast-feeding
Do not use this medicine if you are breast-feeding.

Fertility
Male patients treated with Cisplatin are advised not to father a child during treatment and up to 6 months after treatment. Treatment with cisplatin can potentially cause permanent sterility in men. It is recommended that men who wish to become fathers in the future, seek advice regarding frozen storage (cry conservation) of their sperm prior to treatment.

Driving and using machines
Do not drive or use machines if you experience any side effect which may lessen your ability to do so.

Cisplatin injection contains sodium
This medicine contains 3.5 mg sodium (main component of cooking/table salt) in each ml. This is equivalent to 0.18% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine may be prepared with a solution that contains sodium. This should be taken into additional consideration if you are on low salt (sodium) diet.

3. How to use Cisplatin Injection

Dosage and method of administration

Cisplatin Injection should only be given by a specialist in cancer treatment.
The concentrate is diluted with a sodium chloride solution.
Cisplatin is usually given by injection into a vein (an intravenous infusion) over period of 6 to 8 hours.
Supportive equipment should be available to control anaphylactic reactions.
Cisplatin should not come into contact with any materials that contain aluminium.
The recommended dosage of Cisplatin Injection depends on your well-being, the anticipated effects of the treatment, and whether or not cisplatin is given on its own (monotherapy) or in combination with other agents (combination chemotherapy).

Recommended Dose
Cisplatin (monotherapy):
The following dosages are recommended:
- A single dosage of 50 to 120 mg/m² body surface area (BSA), every 3 to 4 weeks.
- 15 to 20 mg/m² per day over a 5-day period, every 3 to 4 weeks

Cisplatin in combination with other chemotherapeutical agents (combination chemotherapy):
- 20 mg/m² area (BSA) or more, once every 3 to 4 weeks.

For treatment of cervical cancer cisplatin is used in combination with radiotherapy or other chemotherapy medicines.
A typical dose is 40 mg/m² BSA weekly for 6 weeks.
In order to avoid, or reduce, kidney problems, you are advised to drink copious amounts of water for a period of 24 hours following treatment with Cisplatin Injection.

If you believe you have received more Cisplatin Injection than you should
Your doctor will ensure that the correct dose for your condition is given. In case of overdose, you may experience increased side effects. Your doctor may give you symptomatic treatment for these side effects. If you think you received too much Cisplatin Injection, immediately contact your doctor.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them

If any of the following happen, tell your doctor immediately:
- severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), flushing, and you may feel you are going to faint
- severe chest pains possibly radiating to the jaw or arm with sweating, breathlessness and nausea (heart attack)
- fainting or fitting
- hearing problems - you may experience ringing in the ears or hearing loss (ototoxicity)
- kidney and urine problems
- excessive tiredness and general feeling of being unwell, which could be symptoms of decreased levels of blood cells (myelosuppression). This would be confirmed with a blood test.

These are serious side effects. You may need urgent medical attention.

Very common: may affect more than 1 in 10 people:
- decrease in bone marrow function (which can affect the production of blood cells)
- decrease in white blood cells, which makes infections more likely (leukopenia)
- decrease in blood platelets, which increases the risk of bruising and bleeding (thrombocytopenia)
- reduction of red blood cells which can cause weakness and your skin to look pale (anaemia)
- reduced level of sodium in the blood
- high temperature

Common: may affect up to 1 in 10 people:
- severe pain or swelling in either of your legs, chest pain, or difficulty breathing (possibly indicating harmful blood clots in a vein)
- fast, irregular or slow heart beats
- sepsis (blood poisoning)

Uncommon: may affect up to 1 in 100 people:
- severe allergic reaction (see above)
- problems with hearing (ototoxicity)
- reduced level of magnesium in the blood
- abnormal sperm production

Rare: may affect up to 1 in 1,000 people:

- increased risk of acute leukaemia
- seizures (fits)
- fainting, headache, confusion and loss of vision
- loss of certain types of brain function, including brain dysfunction characterised by spasms and reduced level of consciousness
- brain dysfunction (confusion, slurred speech, sometimes blindness, memory loss, and paralysis)
- heart attack
- inflammation of mucous membranes of the mouth (stomatitis).
- peripheral neuropathy of the sensory nerves, characterised by tickling, itching or tingling without cause and sometimes with loss of taste, touch, sight, sudden shooting pains from the neck through the back and into the legs when bending forward

Very rare: may affect up to 1 in 10,000 people:
- heart arrest

Not known: frequency cannot be estimated from the available data:
- signs of infection such as fever or sore throat
- haemolytic anaemia
- inappropriate release of vasopressin hormone (ADH) which may lead to low sodium in the blood and water retention
- blood amylase (enzyme) increased
- dehydration
- reduced level of calcium, phosphate, potassium in the blood
- high level of uric acid in the blood
- muscle cramping
- spinal disease which may cause a sensation of electric shocks passing into your limbs
- loss of taste
- problems with your eyesight (blurred vision, odd colours, loss of vision or eye pain)
- ringing in the ears or deafness
- heart problems
- unusually cold or white hands and feet
- tingling, numbness or tremor in your hands, feet, arms or legs
- persistent headache
- feeling or being sick
- loss of appetite, anorexia
- hiccups
- diarrhoea
- liver enzymes increased, bilirubin increased
- difficulty breathing
- shortness of breath, chest pain particularly upon breathing in, and coughing up blood
- problems with your kidneys or urine
- hair loss
- rash
- extreme tiredness/weakness
- swelling or soreness where the injection was given
- cramps or spasms
- burning or prickling sensation
- unexpected bruising or bleeding
- haemolytic uraemic syndrome which may cause changes to the kidneys and blood

Cisplatin may lead to problems with your blood, liver and kidneys. Your doctor will take blood samples to check for these problems and to monitor electrolytes.

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 Cisplatin Injection

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

Keep container in the outer carton in order to protect from light. Do not refrigerate or freeze.

If a crystal or precipitate has formed as a result of exposure to low temperatures, redissolve by keeping the vials at room temperature till clear solution is obtained.
The product should be discarded if the solution doesn't become clear after vigorous shaking

Do not use this medicine after the expiry date which is stated on the vial and the outer 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.

All materials that have been used for the preparation and administration, or which have been in contact with cisplatin in any way, must be disposed of according to local cytotoxic guidelines

If you find the solution cloudy or a deposit that does not dissolve is noticed, the bottle should be discarded.

6. Contents of the pack and other information

What Cisplatin Injection contains:
Cisplatin Injection contains the active ingredient cisplatin.

Each millilitre (ml) of solution contains 1 milligram (mg) of cisplatin. This medicine is presented in amber glass containers called vials.

Presentations	10 ml	25 ml	50 ml	100 ml
Amount of cisplatin	10 mg	25 mg	50 mg	100 mg

It is available in packs containing a single vial (not all the presentations mentioned may be marketed).

The other ingredients include water for injections, sodium chloride, hydrochloric acid (for pH adjustment) and/or sodium hydroxide (for pH adjustment).

What Cisplatin Injection looks like and content of the pack:
Cisplatin Injection is clear, colourless to pale yellow solution in an amber glass vial practically free from particles with flip off transparent seal.

Packaging with 1 injection vial of 10 ml, each injection vial containing 10 mg cisplatin.
Packaging with 1 injection vial of 25 ml, each injection vial containing 25 mg cisplatin.
Packaging with 1 injection vial of 50 ml, each injection vial containing 50 mg cisplatin.
Packaging with 1 injection vial of 100 ml, each injection vial containing 100 mg cisplatin.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Accord Healthcare Ireland Limited
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

Manufacturer:

Accord Healthcare Polska Sp.z o.o.,
ul. Lutomierska 50,95-200 Pabianice, Poland

Accord Healthcare Single Member S.A.
64th Km National Road Athens,
Lamia, 32009,
Greece

This medicinal product is authorised in the Member States of the European Economic Area and in the United Kindgom (Northern Ireland) under the following names:

Name of the Member State	Name of the medicinal product
Austria	Cisplatin Accord 1 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium	Cisplatin Accord Healthcare 1 mg/ml Solution à Diluer pour Perfusion / concentraat voor oplossing voor infusie / Konzentrat zur Herstellung einer Infusionslösung
Bulgaria	Cisplatin Accord 1 mg/ml Concentrate for Solution for Infusion
Denmark	Cisplatin Accord
Estonia	Cisplatin Accord 1 mg/ml
Finland	Cisplatin Accord 1 mg/ml Infuusiokonsentraatti, Liuosta Varten
Germany	Cisplatin Accord 1 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Hungary	Cisplatin Accord 1 mg/ml Concentrate for Solution for Infusion
Ireland	Cisplatin 1 mg/ml Concentrate for Solution for Infusion
Italy	Cisplatin Accord Healthcare 1 mg/ml Concentrato per soluzione per infusion
Latvia	Cisplatin Accord
Lithuania	Cisplatin Accord 1 mg/ml koncentratas infuziniam tirpalui
The Netherlands	Cisplatin Accord 1 mg/ml Concentraat voor Oplossing voor Infusie
Norway	Cisplatin Accord 1 mg/ml Konsentrat til infusjonsvæke
Poland	Cisplatinum Accord
Portugal	Cisplatin Accord
Romania	Cisplatină Accord 1 mg / ml concentrat pentru soluție perfuzabilă
Slovenia	Cisplatin Accord 1 mg/ml koncentrat za raztopino za infundiranje
Spain	Cisplatino Accord 1 mg/ml concentrado para solución para perfusión
Sweden	Cisplatin Accord 1 mg/ml Koncentrat till Infusionsvätska, Lösning
United Kingdom (Northern Ireland)	Cisplatin 1 mg/ml Concentrate for Solution for Infusion

This leaflet was last revised in 05/2024.

(Please note this is a Prescriber Information Leaflet NOT the SPC. For full details regarding this product please refer to the SPC.)

The following information is intended for medical or healthcare professionals only:

Preparation and handling of the product
Like with all anti-neoplastic products caution is needed with the processing of cisplatin. Dilution should take place under aseptic conditions by trained personnel in an area specifically intended for this. Protective gloves should be worn for this. Precautions should be taken to avoid contact with the skin and mucous membranes. If skin contact did occur anyway, the skin should be washed with soap and water immediately. With skin contact tingling, burns and redness have been observed. In case of contact with the mucous membranes they should be copiously rinsed with water. After inhalation dyspnoea, pain in the chest, throat irritation and nausea have been reported.

Pregnant women must avoid contact with cytostatic drugs. Cisplatin should not be used during pregnancy unless the clinician considers the risk in an individual patient to be clinically justified.

Bodily waste matter and vomit should be disposed with care.

If the solution is cloudy or a deposit that does not dissolve is noticed, the bottle should be discarded.

A damaged bottle must be regarded and treated with the same precautions as contaminated waste. Contaminated waste must be stored in waste containers specifically marked for this. See section "Disposal".

Preparation of the intravenous administration
Take the quantity of the solution that is needed from the bottle and dilute with at least 1 litre of the following solutions:

- sodium chloride 0.9%
- mixture of sodium chloride 0.9% / glucose 5% (1:1), (resulting final concentrations: sodium chloride 0.45%, glucose 2.5%)
- sodium chloride 0.9% and 1.875% mannitol, for injection
- sodium chloride 0.45%, glucose 2.5% and 1.875% mannitol for injection

Always look at the injection before use. Only a clear solution, free from particles should be administered.

If precipitate or crystal observed inside the vial, keep vial at room temperature (20 - 25°C) until till clear solution obtained. Protect unopened container from light. The product should be discarded if the solution doesn't become clear after vigorous shaking.

DO NOT bring in contact with injection material that contains aluminium.
DO NOT administer undiluted.
With respect to microbiological, chemical and physical stability with use of the undiluted solutions, see below "Special precautions for storage".

Although cisplatin is usually administered intravenously, the drug has also been given by intraperitoneal instillation to patients with intraperitoneal malignancies (e.g., ovarian tumours). Steep concentration gradients between intraperitoneal and plasma drug levels can be achieved by this route of administration.

Disposal
All materials that have been used for the preparation and administration, or which have been in contact with cisplatin in any way, must be disposed of according to local cytotoxic guidelines. Medicines should

not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Incompatibilities
Do not bring in contact with aluminium. Cisplatin may interact with metal aluminium to form a black precipitate of platinum. All aluminium-containing IV sets, needles, catheters and syringes should be avoided.

Cisplatin decomposes with solution in media with low chloride content; the chloride concentration should at least be equivalent to 0.45% of sodium chloride.
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Antioxidants (such as sodium metabisulphite), bicarbonates (sodium bicarbonate), sulfates, fluorouracil and paclitaxel may inactivate cisplatin in infusion systems.

Special precautions for storage
Medicinal product as packaged for sale:

Concentrate for solution for infusion 1 mg/ml
Undiluted solution: Keep container in the outer carton in order to protect from light. Do not refrigerate or freeze. If the solution is not clear or an undissolvable precipitate is formed the solution must not be used.

Diluted solution:
For the storage condition of the diluted medicinal product: see below
“Concentrate for solution for infusion after dilution”.
Do not refrigerate or freeze.

Concentrate for solution for infusion after dilution:
After dilution
Chemical and physical in-use stability after dilution with infusion fluids described in section “Preparation and handling of the product”, indicate that after dilution with recommended intravenous fluids, Cisplatin Injection remains stable for 24 hours at 20 - 25 °C room temperature.
From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and dilution should taken place in controlled and validated aseptic conditions.