

PACKAGE LEAFLET: INFORMATION FOR THE USER

CARDIOXANE® 500 mg powder for solution for infusion Dexrazoxane

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

- 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 Cardioxane is and what it is used for
2. Before you are given Cardioxane
3. How Cardioxane is used
4. Possible side effects
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1. WHAT CARDIOXANE IS AND WHAT IT IS USED FOR

Cardioxane contains a substance called dexrazoxane. This substance belongs to a group of medicines which protect the heart (cardioprotective medicines).

Cardioxane is used to prevent heart damage when medicines called doxorubicin or epirubicin are used during breast cancer treatment in adults.

2. BEFORE YOU ARE GIVEN CARDIOXANE

You must not be given Cardioxane

- If you are under 18 years old.
- If you are allergic (hypersensitive) to dexrazoxane.
- If you are breast-feeding (see also "Pregnancy and breast-feeding").

If any of the above apply, you must not be given this medicine.

Before you are given Cardioxane, tell your doctor

- If you have or have had liver or kidney problems.
- If you have or have had a heart attack, heart failure, uncontrolled chest pain and heart valve problems.
- If you are pregnant or plan to become pregnant (see also "Pregnancy and breast-feeding").
- If you are allergic to dexrazoxane or razoxane.

You should also be aware that:

- Your doctor may carry out tests before and during the treatment with Cardioxane to see how well the treatment is working and to check the function of some of your organs, such as your heart, kidneys or liver.
- Your doctor may carry out blood tests during the treatment with Cardioxane to monitor your bone marrow function. If you are receiving high-dose cancer treatment (e.g. chemotherapy or radiation) and are also being treated with high doses of Cardioxane, your bone marrow function may be reduced. This may affect the production of red blood cells, white blood cells, and platelets.

- Cardioxane may increase the risk of developing leukaemia (cancer of the blood).
- During treatment with Cardioxane, women of childbearing potential and men should use effective contraception. Men should continue using contraception for at least three months after Cardioxane treatment has been stopped (see also “Pregnancy and breast-feeding”).
- The combination of Cardioxane with your cancer treatment may increase the risk of blood clots.
- **If Cardioxane powder or solution gets on your skin**, tell your doctor straight away. You or your doctor should immediately rinse the affected area thoroughly with water.

Taking other medicines

Please tell 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

- You will not be given Cardioxane if you are pregnant or had planned to become pregnant, unless your doctor decides it is necessary.
- Women of childbearing potential should use effective contraception during treatment with Cardioxane.
- Men should use effective contraception during treatment with Cardioxane and for at least three months after Cardioxane treatment has been stopped.
- Stop breast-feeding while you are receiving Cardioxane treatment.

Ask your doctor or pharmacist for advice before taking any medicine while you are pregnant or breast-feeding.

Driving and using machines

Tiredness has been reported with Cardioxane treatment. Therefore if you feel sleepy, do not drive or use machines.

3. HOW CARDIOXANE IS USED

How Cardioxane is given to you

This medicine is prepared and given to you by your doctor or other medical staff. The dose you will receive is decided by your doctor.

- Cardioxane is given as a drip (infusion) into a vein over about 15 minutes.
- This will start approximately 30 minutes before your cancer treatment (doxorubicin and/or epirubicin).

If you think you have been given more Cardioxane than you should

If you are given too much Cardioxane, tell your doctor or nurse straight away. You may experience some of the side effects listed in section 4, “Possible side effects”.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Cardioxane can have side effects, although not everybody gets them.

Some side effects can be serious and need immediate medical attention:

Very common (affecting more than 1 in 10 patients):

- Frequent infections, fever, sore throat, unexpected bruising and bleeding (signs of blood disorders such as low red blood cell counts, low white blood cell counts, low level of platelets and low levels of granulocytes. Your blood counts may however return to normal after each treatment cycle).

Common (affecting less than 1 in 10 patients):

- Swelling and reddening of a vein.

Uncommon (affecting less than 1 in 100 patients):

- Leukaemia (cancer of the blood).
- Sudden loss of consciousness.
- Swelling and pain in one part of the body that can be caused by blood clotting within vein.
- Tissue swelling in limbs.

The following side effects have been reported in very few patients during treatment with Cardioxane:

- Allergic reactions including itching, rash, facial/throat swelling, wheezing, breathlessness or difficult breathing, changes in levels of consciousness, hypotension.
- Sudden onset of shortness of breath, coughing up blood and chest pain (signs of blood clot in the lung).

If you get any of the above, tell your doctor straight away or go to the nearest emergency unit.

Other side effects include:

Very common (affecting more than 1 in 10 patients):

- Hair loss.
- Vomiting, mouth sores, nausea.
- Weakness.

Common (affecting less than 1 in 10 patients):

- Diarrhoea, stomach pain, constipation, fullness in stomach and loss of appetite.
- Decreased heart muscle function, fast heart beat.
- Pain, redness and swelling of the moist lining of the internal passageways such as the airways or food pipe.
- Nail disorders such as blackening.
- Skin reaction such as swelling, redness, pain, burning sensation, itching at the site of injection.
- Tingling or numbness of the hands or feet, dizziness, headache.
- Discharge from the eye with itching, redness and swelling.
- Tiredness, generally feeling unwell.
- Slight fever.
- Abnormal liver function test results.

Uncommon (affecting less than 1 in 100 patients)

- Increase in blood cell counts.
- Vertigo, ear infection.
- Bleeding, tender or enlarged gums, oral thrush.
- Thirst.

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

5. HOW TO STORE CARDIOXANE

- Do not store above 25°C. Store in the original package in order to protect from light.
- Do not use Cardioxane after the expiry date which is stated on the pack.
- 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.

6. FURTHER INFORMATION

What Cardioxane contains

- The active substance is dexrazoxane (as dexrazoxane hydrochloride).
- Each vial contains 500 mg of dexrazoxane. Cardioxane contains no other ingredients.

What Cardioxane looks like and contents of the pack

Cardioxane is a white to off-white powder for solution for infusion available in packs of one vial and packs of four vials. Not all pack sizes may be marketed in your country.

Marketing Authorisation Holder

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For any information about this medicinal product, please contact the Marketing Authorisation Holder.

This leaflet was last approved in August 2012.

INFORMATION FOR HEALTHCARE PROFESSIONALS

CARDIOXANE 500 mg powder for solution for infusion

Dexrazoxane

POSOLOGY AND METHOD OF ADMINISTRATION

Cardioxane is administered by a short intravenous infusion (15 minutes), approximately 30 minutes prior to anthracycline administration at a dose equal to 10 times the doxorubicin-equivalent dose level and 10 times the epirubicin-equivalent dose.

Thus it is recommended that Cardioxane is given at a dose of 500 mg/m² when the commonly used dosage schedule for doxorubicin of 50 mg/m² is employed or 600mg/m² when the commonly used dosage schedule for epirubicin of 60 mg/m² is employed.

Paediatric population

Cardioxane is contraindicated in children and adolescents up to 18 years of age.

Renal impairment

In patients with moderate to severe renal dysfunction (creatinine clearance < 40 ml/min) the dexrazoxane dose should be reduced by 50%.

Hepatic impairment

The dose ratio should be kept, i.e. if the anthracycline dose is reduced the dexrazoxane dose should be reduced accordingly.

In case of overdose, symptomatic treatment should be provided.

INSTRUCTIONS FOR USE

Recommendations for safe handling

Prescribers should refer to national or recognised guidelines on handling cytotoxic agents when using Cardioxane. Reconstitution should only be carried out by trained staff in a cytotoxic designated area. The preparation should not be handled by pregnant staff.

Use of gloves and other protective clothing to prevent skin contact is recommended. Skin reactions have been reported following contact with Cardioxane. If Cardioxane powder or solution comes into contact with the skin or mucosal surfaces, the affected area should immediately be rinsed thoroughly with water.

Preparation for intravenous administration

Reconstitution of Cardioxane

For reconstitution the contents of each vial should be dissolved in 25 ml of water for injections. The vial contents will dissolve within a few minutes with gentle shaking. The resultant solution has a pH of approximately 1.6. This solution should be further diluted before administration to the patient.

Dilution of Cardioxane

To avoid the risk of thrombophlebitis at the injection site, Cardioxane must be diluted prior to infusion with one of the solutions mentioned in Table 1. The final volume is proportional to the number of Cardioxane vials used and the amount of infusion fluid for dilution, which can be between 25 ml and 100 ml per vial.

Table 1. below summarises the final volume and the approximate pH of reconstituted and diluted product for one vial and four vials of Cardioxane. The minimum and maximum volumes of infusion fluids to be used per vial are shown in Table 1.

Table 1. Reconstitution and dilution of Cardioxane vials

Infusion fluid used for dilution	Volume of fluid used to dilute 1 vial of reconstituted Cardioxane	Final volume from 1 vial	Final volume from 4 vials	pH (approximate)
Ringer lactate	25 ml	50 ml	200 ml	2.2
	100 ml	125 ml	500 ml	3.3
0.16 M sodium lactate*	25 ml	50 ml	200 ml	2.9
	100 ml	125 ml	500 ml	4.2

* Sodium lactate 11.2% should be diluted by a factor of 6 to reach a concentration of 0.16 M

The use of larger dilution volumes (with a maximum of 100 ml of additional infusion fluid per 25 ml reconstituted Cardioxane) is usually recommended to increase the pH of the solution. Smaller dilution volumes (with a minimum of 25 ml of additional infusion fluid per 25 ml reconstituted Cardioxane) can be used if needed, based on the haemodynamic status of the patient.

Reconstituted, diluted Cardioxane is for single use only. The diluted solution should be used immediately or stored for not longer than 4 hours between +2°C and +8°C and protected from light.

Parenteral medicinal products should be inspected visually for particulate matter whenever the solution and container permit. Cardioxane is normally a colourless to yellow solution immediately on reconstitution, but some variability in colour may be observed over time, which does not indicate loss of activity if the product has been stored as recommended. It is however recommended to dispose of the product if the colour immediately on reconstitution is not colourless to yellow.

Incompatibilities

Cardioxane must not be mixed with any products other than the solutions for dilution mentioned above.

Storage

Do not use Cardioxane after the expiry date which is stated on the pack.

Before opening

Do not store above 25°C. Store Cardioxane vials in the original package in order to protect from light.

After reconstitution and dilution

The diluted solution of Cardioxane is physically and chemically stable for 4 hours at 25°C.

From a microbiological point of view, the readily prepared infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. These must not exceed 4 hours at 2°C to 8°C (in a refrigerator), protected from light.

Disposal

Any unused solution should be discarded in accordance with local requirements. Adequate care and precaution should be taken in the disposal of items used to reconstitute and dilute Cardioxane.