PACKAGE LEAFLET: INFORMATION FOR THE USER
Doxorubicin 2mg/ml Concentrate for solution for infusion
Referred to in this leaflet as Doxorubicin 2mg/ml
Doxorubicin hydrochloride

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- 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 DOXORUBICIN 2MG/ML IS AND WHAT IT IS USED FOR

Doxorubicin, the active ingredient in Doxorubicin 2 mg/ml, is a medicine that kills cancer cells. It is used to treat several types of cancer, e.g., breast cancer, lung cancer, leukaemia (cancer of the blood or bone marrow), tumours of the thyroid gland, bladder and ovaries, and paediatric malignancy. Doxorubicin 2 mg/ml is frequently used in combination with other anti-cancer treatments.

2. BEFORE YOU USE DOXORUBICIN 2 MG/ML

Do not use Doxorubicin 2 mg/ml
- if you are hypersensitive (allergic) to doxorubicin or any of the other ingredients of Doxorubicin 2 mg/ml, or to other anthracyclines or anthracenediones (anti-cancer medicines)
- if you are pregnant or breastfeeding

Intravenous medication must not be used if:
- you have decreased bone marrow function or if severe oral mucositis (inflammation of the mouth) has occurred during previous cytotoxic therapy
- you have a generalised infection
- you have severe hepatic impairment (liver damage)
- you have severe arrhythmia (irregular heart beat), cardiac impairment (problems with your heart function) or you have had a heart infarction (heart attack)
- you have had prior treatment with anthracycline in excess of a certain cumulative level

Intravesical (placed directly into the bladder through a catheter) medication must not be used if:
- you have a tumour that has penetrated the bladder wall
- you have a urinary tract infection
- you have a bladder infection
- there are problems with catheterisation (insertion of a small plastic tube into the urethra)

Take special care with Doxorubicin 2 mg/ml:
- if you have a bone marrow disease
- if you have decreased bone marrow function
- if you have had prior treatment with anthracycline
- if you have had mediastinal irradiation (radiotherapy in the region between the lungs, where the heart and major blood vessels are located)
- if you have hepatic impairment (liver damage) or blocked bile flow
- if you have severe renal impairment (kidney damage)

Using other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, inform your doctor if you have used the following medicines:
- other anthracyclines
- other preparations with cardiac toxicity (damage to the heart muscles), such as 5-fluorouracil, cyclophosphamide and paclitaxel (anti-cancer medicines)
- preparations that have an effect on cardiac function, such as calcium antagonists
- other preparations with hepatic toxicity, such as 6-mercaptopurine (immunosuppressive medicines)
- cyclosporine (immunosuppressive medicine)
- verapamil (calcium channel blocker used for heart problems)
- digoxin (used in the treatment of abnormal heart rhythms)

Patients should not be vaccinated during treatment with Doxorubicin 2 mg/ml, and they should avoid people who have recently received a live oral polio vaccination.

Taking Doxorubicin 2 mg/ml with food and drink:
Doxorubicin 2 mg/ml may be taken with or without food. If the medicine is administered intravesically, patients should not drink any fluids in the 12 hours prior to instillation.

Pregnancy
Doxorubicin 2 mg/ml should not be used during pregnancy. During pregnancy, cytotoxic agents (chemicals which are harmful to cells) are generally administered only after careful consideration of their benefits to the mother and the risks to the foetus.
Both men and women should use effective contraception during and up to 6 months after treatment.

Breastfeeding
Doxorubicin 2 mg/ml is excreted into breast milk. Breastfeeding should be discontinued for the duration of treatment with doxorubicin.

Driving and using machines
The effect of this medicine on the ability to drive and use machinery has not been studied.

The medicinal product contains 3.54 mg sodium per 1 ml of doxorubicin hydrochloride concentrate for solution for infusion. This should be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE DOXORUBICIN 2 MG/ML

Your doctor will prescribe the dosage and administration route on an individual basis and take care of the practical treatment arrangements.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Doxorubicin 2 mg/ml can cause side effects. Some of these are so severe that the patient should be closely monitored. Nausea and vomiting as well as hair loss occur in almost all patients.

Common (occur in 1 in 100 to 1 in 10 patients):
Blood and lymphatic tissue: Decrease in the white blood cell count, potentially resulting in systemic infections (infections which may affect different organs in the body), which can be severe. If you get a fever or experience other signs of infection after the therapy, seek immediate medical assistance.
Vascular: Cardiomyopathy (heart muscle disorder), ECG changes. Cardiomyopathy may occur a long while after discontinuation of the therapy.
Gastrointestinal: Nausea, vomiting, mucositis (inflammation of the digestive tract), loss of appetite, diarrhoea
Skin and subcutaneous tissue: Hair loss
Administration site conditions: Local reactions (bladder infection) may occur when the medicine is administered intravesically.

Uncommon (occur in 1 in 100 to 1 in 1,000 patients):
Gastrointestinal: When the medicine is used in combination with cytarabine (anti-cancer medicine), colon and particularly caecal (bowel) ulcers and necrosis (death of cells or tissue) have been reported.

Rare (occur in 1 in 10,000 to 1 in 1,000 patients):
General: Sudden allergic reactions, chills, fever, dizziness
Skin and subcutaneous tissue: Hives, rash, local redness in the vein used for the injection, skin and nail darkening and loss of nails.
Eyes: conjunctivitis

Urine may become red during the use of the medicine.

If you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE DOXORUBICIN 2 MG/ML

Keep out of the sight and reach of children.

Store in a refrigerator (+2 ℃ – +8 ℃).
Keep vial in the outer carton in order to protect from light.

Store in an upright position.

For single dose use only.
Any unused solution should be discarded immediately after initial use.
Do not use if deteriorated.
Do not use after the expiry date which is stated on the vial and the carton. The expiry date refers to the last day of the month.

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 Doxorubicin 2 mg/ml contains

1 ml of Doxorubicin 2 mg/ml contains 2 mg of the active substance doxorubicin hydrochloride.

- Each 5ml vial contains 10 mg Doxorubicin hydrochloride.
- Each 10ml vial contains 20 mg Doxorubicin hydrochloride.
- Each 25ml vial contains 50 mg Doxorubicin hydrochloride.
- Each 50ml vial contains 100 mg Doxorubicin hydrochloride.
- Each 100ml vial contains 200 mg Doxorubicin hydrochloride.

The product contains sodium chloride (3.54 mg sodium per 1 ml).

The other ingredients are sodium chloride, hydrochloric acid and water for injections.

What Doxorubicin 2 mg/ml looks like and contents of the pack

Doxorubicin 2 mg/ml is a red, clear concentrate for solution for infusion.

It is available in the following pack sizes:
Glass vial, type I glass.
Pack sizes: 5 ml, 10 ml, 25 ml, 50 ml and 100 ml.
Not all pack sizes may be marketed.

Marketing Authorisation Holder in the UK:
Seacross Pharmaceuticals Ltd.
Bedford Business Centre
61 - 63 St Peters Street
Bedford MK40 2PR
United Kingdom

Marketing Authorisation Holder in the IE:
Seacross Pharma (Europe) Ltd.
Skybridge House
Corballis Road North
Dublin Airport, Swords
Co. Dublin, K67 P6K2

Ireland

Manufacturer in the UK:
Seacross Pharmaceuticals Ltd.
Stanmore Place
Howard Road
Stanmore HA7 1BT
United Kingdom

Manufacturer in the IE:
Seacross Pharma (Europe) Ltd.
Skybridge House
Corballis Road North
Dublin Airport, Swords
Co. Dublin, K67 P6K2
Ireland

This medicinal product is authorised in the Member States of the EEA under the following names:

UK: Doxorubicin 2 mg/ml Concentrate for solution for infusion
IE: Doxorubicin 2 mg/ml Concentrate for solution for infusion

This leaflet was revised in 05/2022

DOXORUBICIN 2 MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION

Please read this information carefully before using Doxorubicin and refer to the Summary of Product Characteristics (SPC) for full details.

PRESENTATION

Vials of doxorubicin hydrochloride concentrate for solution for infusion 10mg/5ml, 20mg/10ml, 50mg/25ml, 100mg/50ml and 200mg/100ml. Excipients: Hydrochloric acid, Sodium chloride and Water for injections.

DOSAGE AND METHOD OF ADMINISTRATION

Treatment with Doxorubicin should be supervised by a doctor with extensive experience of cytostatics.

Intravenous administration: The concentrate is injected via the tubing of a freely-running intravenous infusion (Sodium chloride 0.9% intravenous infusion or Dextrose 5% intravenous infusion) over 2-15 minutes. This technique minimizes the risk of thrombophlebitis or perivenous extravasation which can lead to severe cellulitis and vesication. Several dosage regimens exist: The recommended dose is 60-75 mg/m ²body surface i.v. as a single dose or in divided doses on 2-3 consecutive days administered with 21 day's intervals. The lower dose should be given to patients with bone marrow depression. When Doxorubicin is administered in combination with other cytostatics, the dosage should be reduced to 30-60 mg/m ². In patients, who cannot receive the full dose, an alternative dosage is 15-20 mg/m ²body surface per week**.** In order to avoid cardiomyopathy, it is recommended that the cumulative total lifetime dose of doxorubicin (including related drugs such as daunorubicin) should not exceed 450-550mg/m^2 body surface area; 450

mg/m ²should not be exceeded in cases of previous radiation of mediastinum, previous or concomitant treatment with potentially cardiotoxic agents. Reduced doses should be used in cases of decreased liver function (see SPC). Dosage in children may need to be reduced, please refer to treatment protocols.

Intravesical administration: Doxorubicin can be given by intravesical instillation for treatment of superficial cancer of the bladder and to prevent relapse after transurethral resection (T.U.R). The recommended dose for intravesical treatment of superficial cancer of the bladder is 30-50 mg in 25-50 ml of physiological saline per instillation. The solution should remain in the bladder for 1-2 hours. During this period the patient should be turned 90° every 15 minutes. To avoid undesired dilution with urine the patient should be informed not to drink anything for a period of 12 hours before the instillation. The instillation may be repeated with an interval of 1 week to 1 month.
Treatment control: Prior to start of the treatment it is recommended to measure the liver function and renal function. There is a need to measure/control blood values and uric acid levels. Analysis of LVEF should be performed in order to optimise the heart condition of the patient prior to the start of the treatment and after each accumulated dose of approximately 100 mg/m ².

CONTRAINDICATIONS
Pregnancy, lactation or hypersensitivity to doxorubicin, other anthracyclines or anthracenediones.
Contraindications for intravenous administration: Myelosuppression or severe stomatitis subsequent to previous cytotoxic treatment, general infection, severe impaired liver function, severe arrhythmia, impaired heart function, previous cardiac infarct or previous treatment with anthracyclines with maximal cumulative doses.
Contraindications for intravesical administration: Invasive tumours that have penetrated the bladder (beyond T1), urinary tract infections, inflammation of the bladder or problems with catheterisation.

WARNINGS AND PRECAUTIONS FOR USE
There is a need to follow the treatment control above particularly in at risk patients. Dose reduction may be necessary. See SPC for details. Doxorubicin may potentiate the toxicity of other anticancer chemotherapies or amplify radiation toxicity. A stinging or burning sensation at the site of administration may signify extravasation necessitating discontinuation and restarting in a different blood vessel. Monitor the patient for several weeks. Surgical measures might be necessary. The patient should be informed that the urine might be reddish after administration.

INTERACTIONS
Doxorubicin cardiotoxicity is enhanced by previous or concurrent use of other anthracyclines, or other potentially cardiotoxic drugs or with products affecting cardiac function requiring monitoring of cardiac function. Doxorubicin hepatotoxicity may be enhanced by other hepatotoxic treatments. Doxorubicin used in combination with ciclosporin, cimetidine or phenobarbital might require dose-adjustment. Other interactions have been reported with cyclophosphamide, uric acid levels, digoxin and in recently polio vaccinated patients. Doxorubicin potentiates the effect of radiation therapy and can, even if administered some considerable time after discontinuation of the radiation therapy.

PHARMACEUTICAL PARTICULARS
Incompatibilities with the following products have been reported: Heparin, aminophyllin, cephalotin, dexamethasone, fluorouracil and hydrocortisone. Doxorubicin should not be mixed with any other products without evidence of compatibility. Doxorubicin 2 mg/ml is compatible with sodium chloride 0.9% and dextrose 5%. Shelf life before opening: 18 months.

Store in a refrigerator (2 ℃ - 8 ℃). Keep vial in the outer carton in order to protect from light. Store in an upright position. Any unused portion of the vial should be discarded immediately. The user should follow strict guidelines for the safe handling and disposal of antineoplastic agents.