PACKAGE LEAFLET: INFORMATION FOR THE USER

Doxorubicin Hydrochloride 50 mg Powder for Solution for 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 any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, tell 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 Doxorubicin Hydrochloride Powder for Solution for Injection is and what it is used for

Doxorubicin Hydrochloride Powder for Solution for Injection contains the active substance doxorubicin. Doxorubicin Hydrochloride Powder for Solution for Injection is an anti-cancer medicine. Treatment with an anti-cancer medicine is sometimes called cancer chemotherapy.

Doxorubicin is used in the treatment of certain types of cancer, for example, cancers of the blood (leukaemia), breast, soft tissue, bone, lung and bladder. It is also used in the treatment of some cancers in children. Doxorubicin is often given with other anti-cancer medicines.

2. What you need to know before you use Doxorubicin Hydrochloride Powder for Solution for Injection

You should not be given Doxorubicin Hydrochloride Powder for Solution for Injection if
- you have shown signs of hypersensitivity (severe allergy) to doxorubicin, other similar medicines called anthracyclines or anthracenediones or any of the other ingredients mentioned in section 6, in the past
- your bone marrow is not making enough blood cells (your doctor will check for this using blood tests)
- after your last dose you had a burning sensation in your mouth or mouth ulcers

Warning and Precautions
Please tell your doctor if you have or had any of the following medical conditions or illness if:
- you have any heart problems
- you have liver problems
- the levels of cells in your blood become low (your doctor will check this)
- you have received or are going to have radiation therapy
- you have recently received a vaccine or been in contact with someone who has recently been vaccinated against polio

Before starting or during treatment with Doxorubicin Hydrochloride Powder for Solution for Injection, your doctor may perform the following tests:

- X-rays and a heart tracing (ECG)
- Test for your heart's functions
- Blood test

Other medicines and Doxorubicin Hydrochloride Powder for Solution for Injection
Special care is needed if you are taking, have recently taken or might take any other medicines. This is especially important in case of:

- Other anti-cancer medicines
- The combination of ciclosporin (a medicine used to reduce the activity of the body's immune system) and doxorubicin, which may increase the risk of nervous system side effects
- Drugs that affect the heart's function, e.g. calcium channel blockers
- Digoxin (a drug that used to treat heart conditions)
- Inhibitors of cytochrome P-450 (drugs that stop the substance cytochrome P-450, which is important for detoxification of your body, from working e.g. cimetidine, ciclosporin), and drugs inducing cytochrome P-450 (e.g. rifampicin, barbiturates)
- Phenytoin (a drug used to treat epilepsy)
- Clozapine (a drug used to treat schizophrenia)
- Amphotericin B (a drug used against fugal diseases)
- Ritonavir (a drug used to treat human immunodeficiency virus [HIV[)
- Drugs that lower uric acid levels in your blood to prevent gout

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

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

Pregnancy
Due to the risk of birth defects, women of childbearing potential should use appropriate contraception methods during treatment with doxorubicin. You should not get pregnant during treatment or up to 6 months after treatment with Doxorubicin Hydrochloride Powder for Solution for Injection.

Breast-feeding
Do not breast-feed while you are treated with Doxorubicin Hydrochloride Powder for Solution for Injection. The medicine can be passed onto the baby through the breast milk and might harm them.

Fertility
Men and women taking this medicine may become infertile.
In women, ovulation and menstruation (periods) should return once treatment is stopped, although pre-mature menopause may occur.
If you are a man, you should take adequate precautions to ensure that your partner does not become pregnant during your treatment with doxorubicin or up to 6 months after treatment and to seek advice on freezing your sperm prior to treatment (cryo-preservation) because of the possibility or irreversible infertility due to therapy with doxorubicin.

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

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

3. How to Use Doxorubicin Hydrochloride Powder for Solution for Injection

Doxorubicin Hydrochloride for Solution for Injection should only be given under super vision of a doctor with experience in cancer therapy.

This medicine is given by injection into a vein, by infusion (drip) into an artery or by instillation (using a catheter) into the bladder.

Dose
Your doctor will work out the correct dose of Doxorubicin Hydrochloride Powder for Solution for Injection for you and how often it must be given.

The dose of medicine given to you will depend upon your medical condition, your age, size, blood cell levels, how well your liver is working and whether you are receiving any other anti-cancer medicines. Your doctor will check your blood cell levels and tell how well your liver is working using blood tests.

If you are to be given an instillation of this medicine directly into the bladder, you may be told by your doctor not to drink any fluids for 12 hours before treatment. After the installation you may be asked to change your position frequently to ensure that the medicine comes into contact with all areas of the bladder.

If you are given more Doxorubicin Hydrochloride Powder for Solution for Injection than you should
This medicine will be given to you in a hospital, under the supervision of a doctor. It is unlikely that you will be given too much or too little, however, tell your doctor or nurse if you have any concerns.

Acute overdosing is likely to worsen side effects, particularly the blood and heart effects. In case of overdose your doctor will take appropriate measures, which might include a blood transfusion or being nursed in isolation. Heart disorders may occur up to 6 months after an overdose.

If you miss a dose of Doxorubicin Hydrochloride Powder for Solution for Injection
Your doctor will decide on the duration of your treatment with Doxorubicin Hydrochloride Powder for Solution for Injection. If the treatment is stopped before the advised courses of treatment is finished, the effect of the doxorubicin therapy might be reduced. Ask your doctor for advise if you wish to stop the treatment.

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

4. Possible Side Effects

Like all medicines, Doxorubicin Hydrochloride Powder for Solution for Injection can have 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), and you may feel you are going to faint
- pain at the injection site during or immediately after the injection

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

If any of the following happen, tell your doctor as soon as possible:
- unexpected bruises or bleeding, or symptoms of an infection e.g. fever, chills or achiness (these problems may occur up to 3 weeks after your last treatment)
- painful burning sensation in the mouth, throat or oesophagus (food-pipe). It often develops 5 to 10 days after treatment. The vagina and back passage may also be affected. Ulcers may form which can become infected. It normally gets better after 10 days. It is often worse if you have had radiation treatment to these areas before.
- abnormally fast heart beat or changes to the ECG (heart trace)
- Shortness of breath, cough or wheezing
- Swelling of the ankles
- skin problems (such as inflammation, blisters or skin infection where the affected area may be hot, tender and red)
- pain or redness of the blood vessels
- inflammation of veins or red streaking, along a vein near the injection site
- hardening of the walls of a vein
- blockage of blood vessels caused by blood clots
- reddening of the face (if the injection has been given too quickly)
- hot flushes
- hair loss and beard growth may stop during the time the treatment is given
- dehydration (feeling thirsty)
- feeling or being sick
- diarrhoea
- abdominal pain
- red coloured urine (which is no cause for alarm and is related to the colour of the medicine). You should inform your doctor if this does not clear up within a few days or if you think there is blood in your urine).
- Passing urine is painful and more frequent and there is blood in the urine
- drowsiness
- dizziness
- kidney damage
- excessive irritation to your skin that occurs when doxorubicin is administered after radiation treatment
- paleness due to anaemia
- conjunctivitis (red, sore and itchy eyes) or excessive tear production
- loss of appetite
- weakness
- lifting of the nail from the nail beds
- unusual colouration of the nail beds and skin creases (seen in children)
- liver damage
- high level of uric acid in blood that could lead to gout
- tumour lysis syndrome that may cause high blood levels of potassium, phosphate and uric acid, and low blood levels of calcium

As doxorubicin may affect your heart, your doctor may do tests to monitor your heart function before starting treatment and during or after treatment. Problems with your heart may occur even years after stopping doxorubicin treatment.

Doxorubicin may lead to changes in your blood cells. Your doctor will take blood samples to monitor for these and also to check how well your liver and kidneys are working. Leukaemia (abnormalities of the white blood cells) has been reported when doxorubicin has been given together with some other cancer treatments.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: http://www.hpra.ie/
Email: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Doxorubicin Hydrochloride Powder for Solution for Injection

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

Expiry
Do not use this medicine after the expiry date which is stated on the vial label and carton after 'EXP'. The expiry date refers to the last day of that month.

Storage
Keep the vial in the outer carton, in order to protect from light. Do not store above 25°C.

Single use only. Discard any unused contents.

Doxorubicin is a potent cytotoxic agent which should only be prescribed, prepared and administered by professionals who have been trained in the safe use of the preparation.

Chemical and physical in-use stability has been demonstrated for up to 21 days at 2-8°C. From a microbiological point of view the product 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 not normally be longer than 24 hours when stored at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Once reconstituted, do not use Doxorubicin Hydrochloride Powder for Solution for Injection if you notice that it shows evidence of precipitation or any other particulate matter.

6. Contents of the pack and other Information

What Doxorubicin Hydrochloride Powder for Solution for Injection contains
The active ingredient is doxorubicin hydrochloride. Each vial contains 50 mg doxorubicin hydrochloride. After reconstitution, each millilitre (ml) of solution contains 2 milligrams (mg) of doxorubicin hydrochloride.

The other ingredient is lactose monohydrate.

What Doxorubicin Hydrochloride Powder for Solution for Injection looks like and contents of the pack
Doxorubicin Hydrochloride Powder for Solution for Injection is an orange-red powder for solution for injection (a powder which is made into a solution before being injected). It comes in glass containers called vials.

It is supplied as:
- 1 x 50 mg vial

Marketing Authorisation Holder and Manufacturer
Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, UK

This leaflet was last revised in February 2016

Doxorubicin Hydrochloride 50 mg Powder for Solution for Injection

The following information is intended for medical or healthcare professionals only

Further to the information included in section 3, practical information on the preparation/handling of the medicinal product is provided here.

Incompatibilities
Doxorubicin should not be mixed with heparin since it has been reported that these drugs are incompatible to the extent that a precipitate may form. It should also not be mixed with 5-flouorouracil as degradation may occur. Until specific compatibility data are available, it is not recommended that doxorubicin be mixed with other drugs.

Reconstitution and dilution
Single use only

Discard any unused contents

The contents of the vial should be reconstituted with Water for Injection, sodium chloride 0.9%, or 5% glucose intravenous solution to a solution concentration of 2 mg doxorubicin hydrochloride per ml.

Chemical and physical in-use stability following reconstitution in either sodium chloride 0.9% or Water for Injections in glass or polypropylene containers has been demonstrated for up to 21 days at 2-8ºC. From a microbiological point of view, however, the product 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 not normally be longer than 24 hours when stored at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Cytotoxic Handling Guidelines
Doxorubicin is a potent cytotoxic agent which should only be prescribed, prepared and administered by professionals who have been trained in the safe use of the preparation. The following guidelines should be followed when handling, preparing and disposing of doxorubicin.

Preparation: Reconstitution of powder, transfer to syringes or infusion bags should be carried out in designated areas, preferably a laminar flow station.

Personnel must be adequately protected with suitable clothing, gloves, mask and eye shield.

Pregnant women should be excluded from handling cytotoxic agents.

Contamination: In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline. A bland cream may be used to treat transient stinging of skin. Medical advice should be sought if the eyes are affected.

In the event of spillage treat with 1% sodium hypochlorite solution using a cloth/sponge kept in the designate area. Rinse twice with water. Put all cloths into a plastic bag and seal for incineration.

Disposal: All items used during preparation or administration including syringes, containers, absorbent materials, residual solutions should all be placed in a thick plastic bag and incinerated at 700°C.