PATIENT LEAFLET: INFORMATION FOR THE USER

Epirubicin hydrochloride 2 mg/ml

intravesical solution/solution for injection

epirubicin hydrochloride

Read all of this leaflet carefully before you start taking 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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT EPIRUBICIN IS AND WHAT IT IS USED FOR

Epirubicin is an anti-cancer medicine. Treatment with an anti-cancer medicine is sometimes called cancer chemotherapy.

Epirubicin hydrochloride is used in the treatment of:

- Cancer of the breast
- Cancer of the stomach

Epirubicin is also used to help prevent recurrence of superficial bladder cancer after surgery.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE EPIRUBICIN

Do not use Epirubicin
- if you are allergic to epirubicin hydrochloride or any of the other ingredients of this medicine (listed in section 6), or to other similar medicines (anthracyclines – see below).
- if you have fewer blood cells than normal. Your doctor will check this;
- if you have suffered or currently have problems with your heart;
- if you have been treated with high doses of some other anti-cancer medicines including doxorubicin and daunorubicin which belong to the same group of drugs as epirubicin (called anthracyclines. They have similar side effects (including those effects on the heart).
- if you are breastfeeding
- if you have a severe infection
- if you have severe liver problems

When administrated directly into the bladder (intravesical use) epirubicin must not be used if:
- the cancer has penetrated the bladder wall;
- you have an infection in the urine tract;
- you have pain or inflammation in your bladder;
- your doctor has problems inserting a catheter (tube) into your bladder.
- there is a large volume of urine left in your bladder after you attempt to empty it;
- there is blood in your urine.

Warnings and precautions

Talk to your doctor or pharmacist before using Epirubicin
- to make sure your heart is working properly. Your doctor will check this regularly.
- to make sure the number of cells in your blood does not drop too low. Your doctor will check this regularly.
- to check the level of uric acid in your blood. Your doctor will check this.
- to check the presence of blood in your urine. Your doctor will check this.
- if you have liver disease.
- if you have kidney disease.
- if you have received or are receiving radiotherapy to the chest area.
- if you are experiencing severe inflammation or ulcers in your mouth.
- if you note an uncomfortable feeling near or in the injection site during the infusion (possible leakage in surrounding tissue). Tell your doctor immediately.
- if you are planning to start a family, whether you are male or female. Men and women should use effective contraceptive measures during and for 6 months after stopping treatment. Men are advised to ask for information on the possibility of storing sperm by freezing before the treatment.
- if you suffer from infections or hemorrhages (bleeding). Epirubicin may affect bone marrow. The number of white blood cells in your blood will be reduced, which make you more susceptible to infections (leukopenia). Hemorrhages (thrombocytopenia) may occur more easily. These undesirable effects are temporary. Reduction of white blood cells quantity is greater 10-14 days after administration and usually return to normal 21 days after administration.
- if you received or intend to receive any vaccination.

Other medicines and Epirubicin

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Special care will also be taken if you are taking any of the following medicines:
- other medicines that may affect your heart for example, calcium channel blockers (e.g. verapamil, nifedipine and diltiazem), other cancer treatments such as mitomycin-C, dacarbazine, dactinomycin and possibly cyclophosphamide and radiotherapy.
- other medicines that may affect your liver e.g. barbiturates (drugs used in epilepsy or sleep disorders) and rifampicin (a drug used to treat TB)
- trastuzumab: epirubicin should not be taken within 27 weeks of taking trastuzumab
- cimetidine (a drug used to reduce the acid in your stomach)
- paclitaxel and docetaxel (drugs used in some cancers)
- interferon alpha-2b (a drug used in some cancers and lymphomas and for some forms of hepatitis)
- quinine (a drug used for treatment of malaria and for leg cramps)
- dexrazoxane (a drug sometimes used with doxorubicin to reduce the risk of heart problems)
- dexverapamil (a drug used to treat some heart conditions).
- Live or live-attenuated vaccines

Pregnancy, breast-feeding and fertility

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

Epirubicin can cause severe harm to the unborn baby and effective contraception should be used during and until 6 months after treatment with this medicine.

If you are pregnant or become pregnant while receiving epirubicin, you should inform your doctor immediately.

You must not use epirubicin if you are breast-feeding.

Male patients may wish to seek advice on sperm preservation before treatment starts and should use effective contraceptive methods during treatment.
Male patients are advised not to father a child during and for 6 months after stopping epirubicin treatment.

Epirubicin may cause lack of menstrual cycles or premature menopause in premenopausal women.

Driving and using machines

You may feel and/or be sick after being given this medicine, therefore special care should be taken when driving or using machines.

3. HOW TO USE EPIRUBICIN

The dose of medicine given to you will depend on the type of cancer you have, your health, how well your liver is working and any other medicines you may be taking.

Administration directly into a vein (injection or infusion)

The medicine will be given to you as an injection into a vein oven 3-5 minutes. Or it may be diluted with glucose (sugar solution) or sodium chloride (salt water) before it is given slowly, usually via a drip into a vein over 30 minutes. If the drip comes loose or the solution is leaking from the vein, you must tell the nurse or doctor immediately. You may be given another dose of this medicine in 3 weeks.

By being put into the bladder (intravesical administration)

Epirubicin may be administrated directly in the bladder using a catheter. If this method is used, you should not drink any fluids for 12 hours before the treatment so that your urine will not dilute the medicine too much. The medicine solution should be kept in your bladder for 1 hour after being given. Occasionally you will need to alter your position to ensure that the medicine reaches all parts of your bladder.
When emptying your bladder after the medicine has been given, take care that your urine does not come in contact with your skin. In case contact does happen, thoroughly wash the affected area with soap and water but do not scrub.

While you are receiving Epirubicin your doctor will take regular blood tests. This is to measure the effect the drug is having. Your doctor will also do regular tests on how your heart is working.

If the medicine has been added to a bag of fluid for injection, or to be given into the bladder, it should be labelled with the strength of the drug, volume and time after which it should not be used.

If you use more Epirubicin than you should

As this medicine will be given to you while you are in hospital it is unlikely that you will be given too little or too much. However, tell your doctor or pharmacist if you have any concerns.

4. POSSIBLE SIDE EFFECTS

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

The following information is intended for healthcare professionals only:

Epirubicin 2 mg/ml Solution for Injection

epirubicin hydrochloride

FOR INTRAVENOUS INJECTION OR INTRAVESICAL ADMINISTRATION

Incompatibilities

Prolonged contact with any solution of an alkaline pH should be avoided as it will result in hydrolysis of the drug, which includes sodium bicarbonate containing solutions. Only the diluents detailed in “Dilutions Instructions” should be used.

Neither injection nor any diluted solutions should be mixed with any other drugs. Epirubicin should not be mixed with heparin due to physical incompatibility (precipitation).

Dilutions Instructions

The injection may be given via the tubing of a free-running saline infusion. Where the injection is to be administrated after dilution, the following instruction should be followed.

Epirubicin Hikma may be further diluted under aseptic conditions in Glucose 5% or Sodium Chloride 0.9% and administered as an intravenous infusion.
The infusion solution should be prepared immediately before use.

The injection solution contains no preservative and any unused portion of the vial should be discarded immediately.

Safe Handling

This is a cytotoxic product, please follow your local policy guidelines for instructions on the safe handling/disposal of cytotoxics.

If any of the following rare side effects occur when Epirubicin is given by infusion into a vein, tell your doctor immediately:
- if there is any redness, pain or swelling where the injection has been given
- if you have chest pains, shortness of breath or swelling of your ankles (these effects may occur up to several weeks after finishing treatment with epirubicin)
- if you have a severe allergic reaction, noticed by feeling faint, skin rash, swelling of the face and difficulty in breathing or wheeze. In some cases collapse may occur.

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

You may notice other side effects after the medicine has been given into a vein. If you experience any of the following tell your doctor as soon as possible:

Very common (occurs in more than 1 of 10 users)
- inhibition of blood cell production in bone marrow (myelosuppression)
- decreasing of the number of white blood cells (leukopenia)
- decreasing in the number of certain types of white blood cells (granulocytopenia and neutropenia)
- neutropenia with fever (febrile neutropenia)
- decreasing of red blood cells (anemia)
- loss of hair
- reduced growth of facial hair
- red coloration of urine for 1 to 2 days after administration

Common (occurs in more than 1 of 100 but less than 1 of 10 users)
- infection
- feeling or being sick (nausea)
- swelling or pain in your mouth
- ulcers on the lips or tongue or under the tongue
- inflammation of the esophagus (esophagitis)
- vomiting
- diarrhoea
- feeling very dry or thirsty (dehydration)
- loss of appetite (anorexia)
- stomach pain
- reddening along the vein used for the injection
- hot flushes
- cough or symptoms of a chest infection
- bladder inflammation with pain during urination (chemical cystitis), sometimes with blood in the urine (hemorrhagic) following intravesical administration (into the bladder)

Uncommon (occurs in more than 1 of 1000 but less than 1 of 100 users)
- decreasing of the number of platelets (thrombocytopenia)
- vein inflammation (phlebitis)
- vein inflammation related to blood clotting (thrombophlebitis)
- bruising or bleeding

Rare (occurs in more than 1 of 10000 but less than 1 of 1000 users)
- acute lymphocytic leukemia, acute myelogenous leukemia
- fever or chills or symptoms of an infection
- hives (urticaria)
- absence of menstruation (amenorrhea)
- weakness or malaise
- dizziness
- reduced or absent sperm in the semen (azoospermia)
- severe allergic reactions (anaphylaxis)
- increased uric acid levels in the blood (hyperuricemia)
- difficulty in breathing (dyspnoea), swelling (oedema), liver increase (hepatomegaly), accumulation of fluid in the abdominal cavity (ascites), pulmonary oedema, accumulation of fluid between thorax and lungs (pleural effusion), gallop rhythm (signs of congestive heart failure); ECG abnormalities, irregular heartbeat (arrhythmias), heart muscle disease (cardiomyophathy); fast heart rhythm (ventricular tachycardia), slow heart rhythm (bradycardia), atrioventricular block, bundle-branch block.
- change in enzyme levels

Not known (cannot be estimated from the available data)
- shock due to blood infection
- blood infection
- pneumonia
- bleeding and tissue oxygen deficiency (hypoxia) as a result of myelosuppression
- eye inflammation (conjunctivitis and keratitis)
- shock, blood clotting (thromboembolism), including pulmonary emboli
- Local toxicity, rash, itch, skin changes, skin redness (erythema), flushes, skin and nail hyperpigmentation, sensitivity to light (photosensitivity), hypersensitivity to irradiated skin (radiation-recall reaction)
- asymptomatic drops in left ventricular ejection fraction

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard or search MHRA Yellow Card in the Google Play or Apple App store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE EPIRUBICIN

Store and transport refrigerated (2ºC - 8ºC). Store in the original container protected from light.
Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after EXP: MM/YYYY. The expiry date refers to the last day of that month.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

Medicinal product subject to restricted medical prescription.

What Epirubicin contains
- The active substance is epirubicin hydrochloride
- The other ingredients are Sodium Lactate (50% solution); Hydrochloric Acid (1N); Sodium Chloride and Water for Injections

Epirubicin is a solution for injection.

What Epirubicin looks like and contents of the pack
Red solution for injection in clear vials (glass type I) with chlorobutyl rubber stoppers and aluminium cap.

10 mg/5 ml: Packs with 1 vial containing 5 ml solution
20 mg/10 ml: Packs with 1 vial containing 10 ml solution
50 mg/25 ml: Packs with 1 vial containing 25 ml solution
200 mg/100 ml: Packs with 1 vial containing 100 ml solution

Not all packs may be marketed.

Marketing Authorisation Holder and Manufacturer

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

Austria	Epirubicin Hikma 2 mg/ml Injektionslösung
France	Epirubicin Hikma, 2 mg/ml Solution intravésicale/solution injectable
Italy	Epirubicina Hikma
Netherlands	Epirubicine Hikma 2 mg/ml Oplossing voor Injectie
Portugal	Epirrubicina Hikma
Spain	Epirrubicina Hikma, 2 mg/ml Solución intravesical e inyectable
United Kingdom	Epirubicin 2 mg/ml Solution for Injection

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Consilient Health

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Storage
Store and transport refrigerated (2ºC - 8ºC)
Store in the original container to protect from light

Chemical and physical stability was demonstrated, after dilution in Sodium Chloride 0.9% or Glucose 5% solution, for 72 hours when stored in a refrigerator. 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 normally not be longer than 24 hours at 2 to 8ºC, unless dilution has taken place in controlled and validated aseptic conditions.