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 injection that contains epirubicin hydrochloride. It belongs to a group of medicines called cytotoxics used for chemotherapy. Epirubicin causes cells that are actively growing, such as cancer cells, to slow or stop their growth and increases the likelihood that they die. This medicine helps to selectively kill the cancer tissue rather than normal, healthy tissue.
- Epirubicin is used to treat a variety of cancers, either alone or in combination with other drugs. The way in which it is used depends upon the type of cancer that is being treated.
- It has been found to be particularly useful in the treatment of cancers of the breast, ovaries, stomach, bowel and lung.
- Epirubicin can also be put directly into the bladder through a tube. This is sometimes used to treat abnormal cells or cancers of the bladder wall. It can be used after other treatments to try and prevent such cells from growing again.

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 EPIRUBICIN

Do not use Epirubicin
- if you are allergic to epirubicin or any of the other ingredients of this medicine (listed in section 6), or similar chemotherapy drugs (anthracyclines or anthracenediones)
- if you have infections affecting multiple organs
- If you have urine infection
- if you have inflammation of the bladder
- if you have invasive tumours penetrating the bladder
- if you have catheterisation problems (your doctor has problems inserting a catheter (tube) into your bladder)
- if you have presence of blood in urine
- if you have decreased ability to produce blood cells leading to low blood cell counts, as it can lower them further
- if you have previously been treated with Epirubicin or similar chemotherapy drugs, as previous treatment with these medicines can increase the risk of side effects
- if you have suffered from recent heart attack, poor functioning of the heart muscle, severe irregular heartbeat pattern, sudden pain in the chest, non-inflammatory disease of the heart muscle or any other severe heart trouble in the past, or are presently receiving treatment for this
- if you have severe liver disease
- if you are pregnant or breast-feeding

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Epirubicin:
- if your liver or kidneys are not working properly
- if you have had or you are due to have any vaccination
- if you are currently suffering from acute toxicities such as
  - acute inflammation of the mouth
  - low white blood cell count
  - low platelet count or
  - infections in general

This will help your doctor decide if this medicine is suitable for you.

Other medicines and Epirubicin:
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, even those obtained without a prescription, particularly the following:
- Cimetidine (a drug usually used to treat stomach ulcers and heartburn). Cimetidine can make the effects of Epirubicin stronger
- Calcium channel blockers (medicines for the heart)
- Quinine (antimalaria drug)
- Antibiotics such as sulphonamide and chloramphenicol
- Antiretroviral (drugs used to treat infection by HIV)
- Diphenylhydantoin (a drug used to treat epilepsy)
- Painkillers such as amidopyrine derivate
- Trastuzumab therapy for treatment of cancer. Your doctor should avoid using Epirubicin for up to 27 weeks after stopping trastuzumab when possible. If Epirubicin is used before this time, careful monitoring of cardiac function is recommended
- Vaccination with a live vaccine should be avoided in patients receiving epirubicin
- Paclitaxel or docetaxel (drugs used to treat cancer). When paclitaxel is given prior to epirubicin, it may increase concentration of epirubicin in blood. However, when paclitaxel and docetaxel are given together and given after epirubicin, they did not affect concentration of epirubicin
- Dexverapamil (used to treat some heart conditions)
- Dexrazoxane (used to prevent chronic cumulative cardiotoxicity caused by epirubicin)
- Interferon α2b (used to treat cancers)

Pregnancy, breast-feeding and fertility
Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being given this medicine. Avoid becoming pregnant while you or your partner is being treated with this medicine. If you are sexually active, you are advised to use effective birth control to prevent pregnancy during treatment, whether you are male or female. It may cause birth defects, so it is important to tell your doctor if you think you are pregnant.

Breast feeding
You should stop breast feeding before starting treatment with this medicine as some of the drug may get into your milk and possibly harm your child.

Fertility
Men: There is a risk of sterility due to therapy with epirubicin and male patients should consider storage of sperm before treatment.

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

Driving and using machines
There are no special precautions, as long as you feel fully recovered following your hospital treatment and you have discussed this with your doctor.

Epirubicin contains sodium
Epirubicin 10 mg/5 ml
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

Epirubicin 20 mg/10 ml
This medicine contains 34.48 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.72% of the recommended maximum daily dietary intake of sodium for an adult.

Epirubicin 50 mg/25 ml
This medicine contains 86.19 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 4.31% of the recommended maximum daily dietary intake of sodium for an adult.

Epirubicin 200 mg/100 ml
This medicine contains 344.73 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 17.24% of the recommended maximum daily dietary intake of sodium for an adult.

3. HOW TO USE EPIRUBICIN

If you are prescribed Epirubicin it will only be given to you by doctors or nurses experienced in giving chemotherapy.

This medicine will normally be given to you by a doctor or a nurse through a drip (infusion) into a vein. Your doctor will decide what dose to give and the number of days' treatment you will receive depending on your condition.

The dose is decided by taking into account the condition you have, your height and weight. From your height and weight the doctor will work out your body surface area, and it is this that your dose is calculated from. Epirubicin can also be put directly into the bladder to treat bladder cancer, or to help prevent it returning. The dose depends on the type of bladder cancer you have. When this medicine is injected directly into the bladder, you will be instructed not to drink any fluid for 12 hours before treatment to avoid dilution of the medicine with urine in your bladder.

While one course of treatment may sometimes be enough, more often your doctor will advise further courses in three or four weeks' time. It may take several courses before your illness is under control and you feel better.

Regular checks by your doctor during Epirubicin treatment
During treatment your doctor will be making regular checks of your:
- **Blood** - to check for low blood cell counts that may need treatment
- **Heart function** - heart damage can occur when high doses of Epirubicin are given. This may not be detected for several weeks, so regular tests may be required during this period
- **Liver** – using blood tests to check that this medicine is not affecting the way it functions in a harmful way
- **Blood uric acid levels** – Epirubicin may increase uric acid levels in the blood, which might cause gout. Another medicine may be given if your uric acid levels are too high

If you receive high doses of Epirubicin
High doses can worsen side effects like sores in the mouth or may decrease the number of white blood cells (which fight infection) and platelets (these help the blood to clot) in the blood. Should this happen, you may need antibiotics or blood

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The following information is intended for healthcare professionals only:

Epirubicin Hydrochloride 2 mg/ml

intravesical solution/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.

transfusions. Mouth ulcers can be treated to make them less uncomfortable as they heal.

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

4. POSSIBLE SIDE EFFECTS

Very common: (may affect more than 1 in 10 people)
- Infections
- Eye inflammation with red eyes and watery eyes
- A low red blood cell count (anaemia) that can leave you feeling tired and lethargic
- White blood cell counts (which fight infection) can drop, which increases the chance of infections and fever; (leukopenia)
- Decreased thrombocytes (platelets in the blood that help the blood to clot) may occur, which could make you bruise or bleed when injured more easily
- Reduction in the number of certain types of white blood cells – granulocytes and neutrophiles (granulocytopenia and neutropenia)
- A reduction in certain types of white blood cells accompanied by fever (febrile neutropenia)
- Inflammation of the transparent part of the eye called cornea
- Hot flushes
- Inflammation of a vein
- Nausea
- Vomiting
- Inflammation of the mucous lining in the mouth
- Diarrhoea
- Hair loss
- Skin lesion
- Red coloured urine for 1 to 2 days after administration of epirubicin
- Absence of menstruation
- Painful inflammation and ulceration of the mucous membranes lining the digestive tract
- Feeling generally unwell
- Fever
- Changes in levels of some liver enzymes
- After direct administration of epirubicicn into the bladder, inflammation (cystitis) is possible

Common: (may affect up to 1 in 10 people)
- Reduced appetite/loss of appetite
- Lose water or body fluids
- Severe cardiac rhythm disorder (ventricular arrhythmia)
- Cardiac impulse conduction disorders
- Certain forms of heart rhythm disorders (AV block, bundle branch block)
- Slow heartbeat (bradycardia)
- Insufficient pumping of blood by the heart which can cause shortness of breath, accumulation of fluid, and abnormal heart rhythm.
- Bleeding
- Redness of the skin
- Pain behind the breastbone, indigestion, and difficulty in swallowing due to inflammation in the oesophagus
- Pain or burning in the gastrointestinal tract
- Inflammation of the mucous membrane of the gastrointestinal tract
- Ulcers in the gastrointestinal tract
- Rash, itching
- Abnormal discolouration of nails
- Skin changes
- Abnormal discolouration of skin
- Frequent urination
- Redness at the infusion site
- Chills
- Local reactions such as burning sensation
- Reduced heart function

Uncommon: (may affect up to 1 in 100 people)
- High fevers, chills, general malaise, possible cold arms or legs due to blood poisoning
- Lung infection (pneumonia)
- Certain types of cancer of the blood (acute lymphatic leukaemia, acute myeloid leukaemia)
- Blockage in a blood vessel
- Swelling and pain in the legs or arms due to inflammation of a blood vessel, possibly including blood clotting
- Blood clots in the lungs which causes chest pain and breathlessness
- Gastrointestinal tract bleeding
- Hives
- Skin redness
- Feeling of weakness

Please contact your doctor or nurse immediately if you notice any of the following side effects. Although they are rare these symptoms can be serious:

Rare: (may affect up to 1 in 1,000 people)
- Sudden life-threatening allergic reaction. Symptoms include sudden signs of allergy such as rash, itching or hives on the skin, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or trouble breathing
- Increased level of uric acid in the blood.
- Heart damage (cardiotoxicity)
- Absence of sperm cells in the sperm
- Light headedness

Not known: (frequency cannot be estimated from the available data)
- Life-threatening condition that occurs when the blood pressure is too low due to blood poisoning (septic shock)
- Life-threatening condition where the blood pressure is too low
- Insufficient oxygen supply to the tissue due to inhibited blood cell production in the bone marrow
- Appearance of dark spots inside the mouth
- Abdominal discomfort
- Skin redness or other reactions similar to scalding when exposed to sunlight or ultraviolet rays
- Changes in the skin where you previously received radiation treatment

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.

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.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

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) for pH adjustment; Sodium Chloride and Water for Injections

Epirubicin is an intravesical solution/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

Marketing Authorisation Holder
Hikma Farmacêutica (Portugal), S.A.
Estrada do Rio da Mó, 8, 8A e 8B
Fervença
2075-906 Terrugem SNT
Portugal
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e-mail: portugalgeral@hikma.com

Manufacturer
THYMOORGAN Pharmazie GmbH
Schiffgraben 23
D-38690 Goslar

Distributed by
Consilient Health (UK) Ltd.
No.1 Church Road,
Richmond upon Thames,
Surrey. TW9 2QE

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

Austria	Epirubicin Hikma 2 mg/ml Lösung zur intravesikalen Anwendung/Injektionslösung
Netherlands	Epirubicine Hikma 2 mg/ml Intravesicale oplossing / Oplossing voor injectie
Portugal	Epirrubicina Hikma
Italy	EpirubinaSoluzione endovescicale/soluzione iniettabile
Belgium	Epirubicine Hikma 2 mg/ml Intravesicale oplossing / Oplossing voor injectie /Lösung zur intravesikalen Anwendung/Injektionslösung/ solution intravésicale /solution injectable
France	Epirubicine Hikma 2 mg/ml solution intravésicale/solution injectable
Spain	Epirrubicina Hikma 2 mg/ml Solución intravesical e inyectable
United Kingdom	Epirubicin hydrochloride 2 mg/ml Intravesical solution/ Solution for Injection

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Consilient Health

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Epirubicin 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.

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.