PATIENT INFORMATION LEAFLET
Epirubicin Hydrochloride 2 mg/ml solution for injection or infusion
Epirubicin Hydrochloride

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 further questions, please 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 Epirubicin Hydrochloride Injection is and what it is used for
2. Before you are given Epirubicin Hydrochloride Injection
3. How Epirubicin Hydrochloride Injection is given to you
4. Possible side effects
5. How to store Epirubicin Hydrochloride Injection
6. Further information

1. What Epirubicin Hydrochloride Injection is and what it is used for

The name of your medicine is ‘Epirubicin Hydrochloride 2 mg/ml solution for injection or infusion’ but in the rest of the leaflet it will be called ‘Epirubicin Hydrochloride Injection’.

What Epirubicin Hydrochloride Injection is
Epirubicin Hydrochloride Injection is an anti-cancer medicine. Treatment with an anti-cancer medicine is sometimes called cancer chemotherapy. Epirubicin Hydrochloride Injection is part of a group of medicines called anthracyclines. These act upon cells that are actively growing, to slow or stop their growth and increase the chance that the cells die.

What Epirubicin Hydrochloride Injection is used for
Epirubicin Hydrochloride Injection 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.

Epirubicin Hydrochloride Injection is used in the treatment of cancers of the breast, and stomach.

When injected into the bladder through a tube, Epirubicin Hydrochloride Injection is used to treat abnormal cells or cancers of the bladder wall. It can also be used after other treatments for prevention of such cells from growing again.

2. Before you are given Epirubicin Hydrochloride Injection

Do not use Epirubicin Hydrochloride Injection if you
- are allergic (hypersensitive) to epirubicin hydrochloride or any of the other ingredients of Epirubicin Hydrochloride Injection (a list of ingredients can be found in Section 6).
- are aware that your blood counts are low, as Epirubicin Hydrochloride Injection can lower them further.
- suffer with or have suffered with severe heart failure in the past or are presently receiving treatment for this.
- have previously been treated with Epirubicin Hydrochloride Injection or similar chemotherapy drugs as previous treatment with these medicines can increase the risk of side effects.
- suffer from an acute severe infection.
- have severe inflammation in the mouth, pharynx, oesophagus and gastro-intestinal tract.
- are breast-feeding.
- have severe liver problems.

Tell your doctor or hospital pharmacist if any of the above applies to you.
In any of the above cases, you should not be given Epirubicin Injection.
Epirubicin Hydrochloride Injection should not be injected into the bladder if:
- you suffer from urinary infection
- there are tumours which penetrate the bladder wall
- your doctor has problems inserting a catheter (tube) into your bladder
- you have an inflammation of the bladder
- you have large volume of urine left in your bladder after you attempt to empty

Take special care with Epirubicin Hydrochloride Injection

Tell your doctor if:
- you have some kidney or liver problems. You should inform your doctor before treatment, as he/she needs to take special care.
- you have had or you are due to have any vaccination.

Your doctor will also be making regular checks
- so that your blood cell counts will not be too low
- to control the levels of uric acid in the blood
- to see that your heart and liver are working normally
- if you have or are to have radiotherapy to the area around the heart.

You should inform your doctor in case you experience swelling and pain in your mouth or mucous membrane.

It is possible that the urine will have a red colour for one or two days after administration.

Using other medicines

Tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Especially:
- Cimetidine (a drug usually used to reduce the acid in the stomach and heartburn). Cimetidine can make the effects of Epirubicin Hydrochloride Injection stronger.
- Paclitaxel and docetaxel (used in some cancers).
- Calcium channel blockers (medicines for the heart).
- Interferon alfa-2b (used in some cancers and lymphoma and for some yellow fever).
- Quinine (used for treatment of malaria and for leg cramps).
- Antibiotics such as sulphonamide and chloramphenicol.
- Antiretroviral (drugs used to treat infection by HIV).
- Diphenylhydantoin (a drug used to treat epilepsy).
- Painkillers such as amidopyrin derivatives.
- Dexrazoxane (sometimes used with doxorubicin in order to decrease the risk of heart problems).
- Dexverapamil (used to treat some heart conditions).
- Other medicines that may affect your liver and/or heart.

Pregnancy and breast-feeding

Epirubicin Hydrochloride Injection may cause birth defects when used during pregnancy, it is important to tell your doctor if you are pregnant or if you become pregnant during treatment. You must not use Epirubicin Hydrochloride Injection during pregnancy unless clearly indicated by your doctor.

If you or your partner are being treated with Epirubicin Hydrochloride Injection effective birth control to prevent pregnancy during treatment and for 6 months after treatment is advised. If pregnancy occurs during treatment, genetic counselling is recommended.

There is a risk of sterility due to therapy with Epirubicin Hydrochloride Injection and male patients should consider storage of sperm before treatment.

Epirubicin Hydrochloride Injection may be harmful to nursing infants, therefore women must stop breast-feeding before starting treatment with Epirubicin Hydrochloride Injection.

Driving and using machines
Epirubicin Hydrochloride Injection may cause episodes of nausea and vomiting, which can temporarily lead to an impairment of the ability to drive or use machines.

Important information about some of the ingredients of Epirubicin Hydrochloride Injection
This medicinal contains less than 1 mmol sodium (23 mg) per ml, i.e. essentially ‘sodium free’.

3. How Epirubicin Hydrochloride Injection is given to you

Epirubicin Hydrochloride Injection will be given to you by a doctor or nurse, either into a vein or directly into your bladder.
Your doctor will decide the correct dose and number of days treatment you receive, this will depend on the type of cancer you have, your health, height, weight, how well your liver is working and any other treatment you may receive.

By injection or infusion into a vein
Epirubicin Hydrochloride Injection may be given as an injection into a vein over 3-5 minutes. It may also be diluted before it is infused slowly, usually via a drip into a vein over 30 minutes.

By being put into the bladder
If the injection is given into the bladder, you should not drink any fluids for 12 hours before treatment so that your urine will not dilute the drug too much. The solution should be kept in your bladder for 1-2 hours after installation. You will need to turn occasionally to make sure all parts of the bladder are exposed to the drug.

Care should be taken to ensure that the contents of the bladder, when emptied, do not come into contact with the skin. In case of skin contact, thoroughly wash the affected area with soap and water but do not scrub.

Your doctor will regularly check your blood for any unwanted effects. To detect any possible heart damage your doctor will also monitor your heart for several weeks after the treatment.

Regular checks by your doctor during Epirubicin Hydrochloride Injection 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 Hydrochloride Injection 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 Hydrochloride Injection 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 more Epirubicin Hydrochloride Injection than you should:

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 transfusions. Mouth ulcers can be treated to make them less uncomfortable as they heal.
Please tell your doctor if you have any concerns.

4. Possible side effects

Like all medicines, Epirubicin hydrochloride Injection can cause side effects, although not everybody gets them.

If any of the following side effects happen when epirubicin is given by infusion into a vein tell you doctor immediately, as these are very serious side effects. You may need urgent medical attention:

- redness, pain or swelling at the injection site; tissue damage may occur after accidental injection outside a vein
- symptoms of heart problems such as chest pain, shortness of breath, swelling of your ankles (these effects may occur up to several weeks after finishing treatment with epirubicin)
- severe allergic reaction, symptoms include faintness, skin rash, swelling of the face and difficulty in breathing or wheeze . In some cases collapse may occur.
If you experience any of the following tell your doctor as soon as possible:

**Very common (these may affect at least 1 in 10 people):**

- White blood cell counts (which fight infection) can drop, which increases the chance of infections and fever.
- A low red blood cell count (anaemia) that can leave you feeling tired and lethargic.
- Hair loss - may be quite severe. Beard growth may stop in men. Hair normally re-grows when your treatment course ends.
- Red discolouration of urine (which is normal and related to the colour of the medicine). You should inform your doctor if it does not stop in a few days or you think there is blood in your urine.

**Common (these may affect between 1 in 100 and 1 in 10 people):**

- Infections
- Allergic reactions,
- Feeling or being sick (nausea or vomiting),
- Diarrhoea (which can result in dehydration),
- Feeling thirsty (dehydration),
- Loss of appetite,
- Abdominal pain,
- Heartburn,
- Inflammation of the gullet (oesophagitis),
- High levels of pigments in the mouth,
- Swelling and pain in your mouth,
- Ulcers involving the lips and/or tongue and/or under the tongue, which may not appear until 3-10 days after treatment
- Hot flushes,
- Changes in blood cells causing bleeding,
- Fever.
- Pain, redness, burning or stinging sensation at injection site
- Irritation of the bladder or damage to the bladder wall (called necrosis)

**Uncommon (these may affect between 1 in 10,000 and 1 in 100 people):**

- Platelets (cells that help the blood to clot) can be affected which could make you bruise or bleed more easily. It is important to seek medical advice if this happens,
- Swelling, redness, leg pain, which can be associated with blood clots.
- Vein inflammation including blood clotting (thrombophlebitis).

**Rare (these may affect between 1 in 10,000 and 1 in 1,000 people):**

- When given in combination with other anti-cancer drugs, some patients have developed a rare leukaemia (cancer of white blood cells) after completing treatment,
- Tiredness, weakness and feeling cold,
- Gasping for air, shortness of breath, swelling of abdomen, legs or ankles, fluid in lungs (signs of congestive heart failure),
- ECG abnormalities, irregular heartbeat, heart muscle disease
- Hives (urticaria),
- Fever and/or chills,
- Dizziness,
- Absence of menstrual periods (amenorrhea),
- Low sperm count,
- Increase uric acid levels in the blood which might cause gout,
- Changes in heart or liver function.
- Fever with an extreme elevation of body temperature (hyperpyrexia)
- Feeling of general discomfort or uneasiness (malaise)

**Not known (cannot be estimated from the available data)**

- Blood infection,
- Pneumonia,
- Internal bleeding,
Inflammation to the eye (conjunctivitis and keratitis),
Shock,
Discolouration of skin and nails,
Sensitive to light,
Blood clots, including a clot in the lungs which causes chest pain and breathlessness.

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.

5. How to store Epirubicin Hydrochloride Injection

Store in a refrigerator (2°C – 8°C). Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Always keep Epirubicin Hydrochloride Injection in a safe place and out of the reach and sight of children.

Do not use Epirubicin Hydrochloride Injection after the expiry date, which is printed on the label and carton after EXP. The expiry date refers to the last day of that month.

Do not use Epirubicin Hydrochloride Injection if you notice any visible signs of deterioration.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose medicines no longer required. These measures will help to protect the environment.

6. Further information

What Epirubicin Hydrochloride Injection contains:

The active ingredient in Epirubicin Injection is Epirubicin Hydrochloride.
Each ml contains 2 mg Epirubicin Hydrochloride.
Other ingredients include sodium chloride, hydrochloric acid and water for injection.

What Epirubicin Hydrochloride Injection looks like and content of the pack:

Epirubicin Injection is a clear, red coloured solution.

Pack sizes:
1 x 5 ml vial (10 mg/5 ml)
1 x 10 ml vial (20 mg/10 ml)
1 x 25 ml vial (50 mg/25 ml)
1 x 50 ml vial (100 mg/ 50 ml)
1 x 100 ml vial (200 mg/100 ml)

5 and 10 ml vials: Type I tubular glass vial with 20 mm chlorobutyl RTS rubber stopper and aluminium flip-off white seal.
25 ml vial: Type I tubular glass vial with 20 mm chlorobutyl RTS rubber stopper and aluminium flip-off white/royal blue seal.
50 ml vial: Type I clear moulded glass vial with 20 mm chlorobutyl RTS rubber stopper and aluminium flip-off royal blue seal.
100 ml vial: Type I clear moulded glass vial with 20 mm chlorobutyl RTS rubber stopper and aluminium flip-off white / royal blue seal.

Pack size: 1 vial.

Not all pack sizes may be marketed

Product license holder:
Accord Healthcare Limited,
Sage House, 319 Pinner Road,
North Harrow,
Manufacturer:
Accord Healthcare Limited,
Sage House, 319 Pinner Road,
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This leaflet was last revised on 02/2019.
The following information is intended for medical or healthcare professionals only:

**Incompatibilities**

Prolonged contact with any solution of an alkaline pH (including bicarbonate containing solutions) should be avoided as it will result in hydrolysis of the drug. Only the diluents detailed in “Instructions for use” should be used. Neither the injection nor any diluted solution should be mixed with any other drugs. A physical incompatibility with heparin has been reported.

Epirubicin should not be mixed with other drugs.

**Instructions for use**

*Intravenous administration:* It is advisable to administer Epirubicin Hydrochloride Injection via the tubing of a freely flowing intravenous infusion (0.9% sodium chloride). To minimize the risk of thrombosis or perivenous extravasation, the usual infusion times range between 3 and 20 minutes depending upon dosage and volume of the infusion solution. A direct push injection is not recommended due to the risk of extravasation, which may occur even in the presence of adequate blood return upon needle aspiration.

*Intravesical administration:* Epirubicin Hydrochloride Injection should be diluted in sterile water for injection or 0.9% sterile saline solution before administration. Epirubicin should be instilled using a catheter and retained intravesically for 1-2 hours. During instillation, the patient should be rotated to ensure that the vesical mucosa of the pelvis receives the most extensive contact with the solution. To avoid undue dilution with urine, the patient should be instructed not to drink any fluid in the 12 hours prior to instillation. The patient should be instructed to void at the end of the instillation.

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

**Guidelines for the safe handling and disposal of antineoplastic agents:**

1. If an infusion solution is to be prepared, this should be performed by trained personnel under aseptic conditions.
2. Preparation of an infusion solution should be performed in a designated aseptic area.
3. Adequate protective disposable gloves, goggles, gown and mask should be worn.
4. Precautions should be taken to avoid the medicinal product accidentally coming into contact with the eyes. In the event of contact with the eyes, irrigate with large amounts of water and/or 0.9% sodium chloride solution. Then seek medical evaluation by a physician.
5. In case of skin contact, thoroughly wash the affected area with soap and water or sodium bicarbonate solution. However, do not abrade the skin by using a scrub brush. Always wash hands after removing gloves.
6. Spillage or leakage should be treated with dilute sodium hypochlorite (1% available chlorine) solution, preferably by soaking, and then water. All cleaning materials should be disposed of as detailed below.
7. Pregnant staff should not handle the cytotoxic preparation.
8. Adequate care and precautions should be taken in the disposal of items (syringes, needles etc) used to reconstitute and/or dilute cytotoxic medicinal products. Any unused product or waste material should be disposed of in accordance with local requirements.

**Storage**

*Product as package for sale:* Store in a refrigerator (2°C – 8°C). Do not freeze.

Keep vial in the outer carton in order to protect from light

**Shelf life after first opening the container:**

The vials are for single use only and any unused portion must be discarded after use. From a microbiological point of view, the product should be used immediately after the first penetration of the rubber stopper. If not used immediately, in use storage times and conditions are the responsibility of the user.

**Shelf life after dilution of the solution for injection:**

The product may be further diluted, under aseptic conditions, in Glucose 5% or Sodium Chloride 0.9% and administered as an intravenous infusion. 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 at 2-8 °C, unless dilution has taken place in controlled and validated aseptic conditions.
Disposal
Medicines should not be disposed of via wastewater or household waste. All material used for preparation, administration or otherwise coming into contact with Epirubicin should undergo disposal according to local guidelines for the handling of cytotoxic compounds.

Please refer to the Summary of Product Characteristics (SPC) for further information about Epirubicin Hydrochloride Injection 2 mg/ml solution for injection or infusion.