For the use of a oncologist or a Hospital or a Laboratory only. 8035104-9093

TORRENCE

Epirubicin Hydrochloride for Injection (Lyophilised)

COMPOSITION

TORRENCE 10

Each vial contains :

Epirubicin Hydrochloride B.P.	10 mg
Methylparaben I.P.	2 mg
Lactose I.P.	q.s.

TORRENCE 50

Each vial contains :

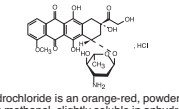
Epirubicin Hydrochloride B.P.	50 mg
Methylparaben I.P.	10 mg
Lactose I.P.	q.s.

DESCRIPTION

Epirubicin Hydrochloride for Injection is a sterile Orange red coloured Lyophilised mass. It contains Methyl Paraben as preservative. Epirubicin hydrochloride is the 4-epimer of doxorubicin and is a semi- synthetic derivative of daunorubicin. It is obtained by chemical transformation of substance produced by certain strain of Streptomyces peucetius.

Epirubicin hydrochloride is (8S, 10S)-10-[(3-amino-2,3,6-trideoxy-α-L-arabino -hexopyranosyl)oxy]- 6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-7,8,9,10-tetrahydrotetracene-5, 12-dione hydrochloride.

The molecular formula of Epirubicin Hydrochloride is $C_{27}H_{29}NO_{11}$.HCl and its molecular weight is 580.0 Its structural formula is :



Epirubicin Hydrochloride is an orange-red, powder.It is soluble in water and in methanol, slightly soluble in anhydrous ethanol; practically insoluble in acetone.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Epirubicin is an anthracycline cytotoxic agent. Although it is known that anthracyclines can interfere with a number of biochemical and biological functions within eukaryotic cells, the precise mechanisms of epirubicin's cytotoxic and/or antiproliferative properties have not been completely elucidated. Epirubicin forms a complex with DNA by intercalation of its planar rings between nucleotide base pairs, with consequent inhibition of nucleic acid (DNA and RNA) and protein synthesis. Such intercalation triggers DNA cleavage by topoisomerase II, resulting in cytocidal activity. Epirubicin also inhibits DNA helicase activity, preventing the enzymatic separation of double-stranded DNA and interfering with replication and transcription. Epirubicin is also involved in oxidation/reduction reactions by generating cytotoxic free radicals. The antiproliferative and cytotoxic activity of epirubicin is thought to result from these or other possible mechanisms.

Pharmacokinetics

In patients with normal hepatic and renal function, plasma levels after intravenous injection of 60-150 mg/m^2 of the drug follow a tri-exponential decreasing pattern with a very fast first phase and a slow terminal phase with a mean half-life of about 40 hours. These doses are within the limits of pharmacokinetic linearity both in terms of plasma clearance values and metabolic pathway. The major metabolites that have been identified are epirubicinol (13-OH epirubicin) and glucuronides of epirubicin and epirubicinol.

The 4'-O-glucuronidation distinguishes epirubicin from doxorubicin and may account for the faster elimination of epirubicin and its reduced toxicity. Plasma levels of the main metabolite, the 13-OH derivative (epirubicinol) are consistently lower and virtually parallel those of the unchanged drug. Epirubicin is eliminated mainly through the liver; high plasma clearance values (0.9 l/min) indicate that this slow elimination is due to extensive tissue distribution. Urinary excretion accounts for approximately 9-10% of the administered dose in 48 hours.

Biliary excretion represents the major route of elimination, about 40% of the administered dose being recovered in the bile in 72 hours. The drug does not cross the blood brain barrier

INDICATIONS

Epirubicin is used in the treatment of a range of neoplastic conditions including;

- Carcinoma of the breast
- Gastric cancer
- Lung cancer

CONTRAINDICATIONS

Epirubicin is contraindicated in:

- Patients who have demonstrated hypersensitivity to the active substance or to any of the excipients, other anthracyclines or anthracenediones.
- Lactation
- Patients with persistent myelosuppression
- Patients with marked myelosuppression induced by previous treatment with either other anti-neoplastic agents or radiotherapy to the mediastinal pericardial area and/or who are under medical treatment with potentially cardiotoxic medicinal products.
- Patients treated with maximal cumulative doses of epirubicin and/or other anthracyclines (e.g. doxorubicin or daunorubicin) and anthracenediones.
- Patients with current or previous history of cardiac impairment and myocardial infraction.
- Patients with acute systemic infections.
- Sever liver impairment.
- Severe arrhythmias
- Unstable angina pectoris
- Myocardiopathy

DOSAGE AND ADMINISTRATION

The safety and efficacy of epirubicin in children has not been established.

Intravenous administration

It is advisable to administer epirubicin via the tubing of a free -running intravenous saline infusion after checking that the needle is properly placed in the vein. Care should be taken to avoid extravasation. In case of extravasation, administration should be stopped immediately.

Conventional dose

When epirubicin is used as a single agent, the recommended dosage in adults is 60-90 mg/m^2 body area. Epirubicin should be injected intravenously over 3-5 minutes. The dose should be repeated at 21-day intervals, depending upon the patient's haematomedullary status. If signs of toxicity, including severe neutropenia/neutropenic fever and thrombocytopenia occur (which could persist at day 21), dose modification or postponement of the subsequent dose may be required.

High dose

Epirubicin as a single agent for the high dose treatment of lung cancer should be administered according to the following regimens:

- Small cell lung cancer (previously untreated): 120 mg/m^2 day 1, every 3 weeks.

For high dose treatment, epirubicin may be given as an intravenous bolus over 3-5 minutes or as an infusion of up to 30 minutes duration.

Breast Cancer

In the adjuvant treatment of early breast cancer patients with positive lymph nodes, intravenous doses of epirubicin ranging from 100 mg/m^2 (as a single dose on day 1) to 120 mg/m^2 (in two divided doses on days 1 and 8) every 3-4 weeks, in combination with intravenous cyclophosphamide and 5-fluorouracil and oral tamoxifen (in accordance with local guidelines) are recommended. Lower doses (60-75 mg/m^2 for conventional treatment and 105-120 mg/m^2 for high dose treatment) are recommended for patients whose bone marrow function has been impaired by previous chemotherapy or radiotherapy, by age, or neoplastic bone marrow infiltration. The total dose per cycle may be divided over 2-3 successive days. The following doses of epirubicin are commonly used in monotherapy and combination chemotherapy for various tumours, as shown:

	Epirubicin Dose (mg/m^2)[a]	
Cancer Indication	Monotherapy	Combination Therapy
Ovarian cancer	60-90	50-100
Gastric cancer	60-90	50
SCLC	120	120

[a] Doses generally given Day 1 or Day 1, 2 and 3 at 21-day intervals

Combination therapy

If epirubicin is used in combination with other cytotoxic products, the dose should be reduced accordingly. Commonly used doses are shown in the table above. In establishing the maximal cumulative doses of Epirubicin (usually: 720 - 1000 mg/m2), any concomitant therapy with potentially cardiotoxic drugs should be taken into account.

Impaired liver function

The major route of elimination of epirubicin is the hepatobiliary system. In patients with impaired liver function the dose should be reduced based on serum bilirubin levels as follows:

Serum Bilirubin	AST*	Dose Reduction
1.4 - 3 mg/100 ml		50%
> 3 mg/100 ml	> 4 times upper normal limit	75%

*AST - aspartate aminotransferase

Impaired renal function

Moderate renal impairment does not appear to require a dose reduction in view of the limited amount of epirubicin excreted by this route. Lower starting doses should be considered in patients with severe renal impairment (serum creatinine > 450µmol/l).

Dose Modifications

Dosage adjustments after the first treatment cycle should be made based on hematologic and nonhematologic toxicities. Dosage adjustments after the first treatment cycle should be made based on hematologic and nonhematologic toxicities. Patients experiencing during treatment cycle nadir platelet counts < 50,000/mm^3, absolute neutrophil counts (ANC) < 250/mm^3, neutropenic fever, or Grades 3/4 nonhematologic toxicity should have the Day 1 dose in subsequent cycles reduced to 75% of the Day 1 dose given in the current cycle. Day 1 chemotherapy in subsequent courses of treatment should be delayed until platelet counts are ≥ 100,000/mm^3, ANC ≥ 1500/mm^3, and nonhematologic toxicities have recovered to ≤ Grade 1.

For patients receiving a divided dose of Epirubicin Hydrochloride for Injection (Day 1 and Day 8), the Day 8 dose should be 75% of Day 1 if platelet counts are 75,000 to 100,000/mm^3 and ANC is 1000 to 1499/mm^3. If Day 8 platelet counts are <75,000/mm^3, ANC <1000/mm^3, or Grade 3/4 nonhematologic toxicity has occurred, the Day 8 dose should be omitted.

Preparation & Administration Precautions

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Procedures normally used for proper handling and disposal of anticancer drugs should be considered for use with Epirubicin Hydrochloride for Injection.

Protective Measures

The following protective measures should be taken when handling Epirubicin Hydrochloride for Injection:

- Personnel should be trained in appropriate techniques for reconstitution and handling.
- Pregnant staff should be excluded from working with this drug.
- Personnel handling Epirubicin Hydrochloride for Injection should wear protective clothing: goggles, gowns and disposable gloves and masks.
- A designated area should be defined for syringe preparation (preferably under a laminar flow system), with the work surface protected by disposable, plastic-backed, absorbent paper.
- All items used for reconstitution, administration or cleaning (including gloves) should be placed in high-risk, waste-disposal bags for high temperature incineration. Spillage or leakage should be treated with dilute sodium hypochlorite (1% available chlorine) solution, preferably by soaking, and then water. All contaminated and cleaning materials should be placed in high-risk, waste-disposal bags for incineration. Accidental contact with the skin or eyes should be treated immediately by copious lavage with water, or soap and water, or sodium bicarbonate solution. However, do not abrade the skin by using a scrub brush. Medical attention should be sought. Always wash hands after removing gloves.

Preparation of Infusion Solution

Reconstitution

Prior to use, Epirubicin Hydrochloride for Injection 10 mg and 50 mg vials must be reconstituted with 5 mL and 25 mL respectively, of Sterile Water for Injection resulting in a solution concentration of 2 mg/mL. Shake vigorously. It may take up to 3 minutes for epirubicin hydrochloride to dissolve completely . It can be further diluted in 5% Glucose solution or 0.9% Sodium Chloride solution and administered as an intravenous infusion.

Reconstituted Solution Stability

From a microbiological point of view, the product should be used immediately. Reconstituted solution is stable for 24 hours at room temperature and for 48 hours in a refrigerator (2^{0}C-8^{0}C). If the solution further diluted with 5% glucose solution or 0.9% Sodium Chloride solution, then it is stable up to 12 hours at 25^{0}C. Do not freeze after reconstitution.

It should be protected from exposure to sunlight. Discard any unused solution.

WARNINGS AND PRECAUTIONS

General

Epirubicin should only be administered under the supervision of a qualified physician who is experienced in the use of cytotoxic therapy. Diagnostic and treatment facilities should be readily available for management of therapy and possible complications due to myelosuppression, especially following treatment with higher doses of epirubicin. Patients should recover from acute toxicities (such as stomatitis, neutropenia, thrombocytopenia, and generalized infections) of prior cytotoxic treatment before beginning treatment with epirubicin. While treatment with high doses of epirubicin (e.g., 90 mg/m^2 every 3 to 4 weeks) causes adverse events generally similar to those seen at standard doses (< 90 mg/m^2 every 3 to 4 weeks), the severity of the neutropenia and stomatitis/ mucositis may be increased. Treatment with high doses of epirubicin does require special attention for possible clinical complications due to profound myelosuppression.

Cardiac Function

Cardiotoxicity is a risk of anthracycline treatment that may be manifested by early (i.e., acute) or late (i.e., delayed) events.

Early (i.e., Acute) Events. Early cardiotoxicity of epirubicin consists mainly of sinus tachycardia and/or electrocardiogram (ECG) abnormalities such as non-specific ST-T wave changes. Tachyarrhythmias, including premature ventricular contractions, ventricular tachycardia, and bradycardia, as well as atrioventricular and bundle-branch block have also been reported. These effects do not usually predict subsequent development of delayed cardiotoxicity, are rarely of clinical importance, and are generally not a consideration for the discontinuation of epirubicin treatment.

Late (i.e., Delayed) Events. Delayed cardiotoxicity usually develops late in the course of therapy with epirubicin or within 2 to 3 months after treatment termination, but later events (several months to years after completion of treatment) have also been reported. Delayed cardiomyopathy is manifested by reduced left ventricular ejection fraction (LVEF) and/or signs and symptoms of congestive heart failure (CHF) such as dyspnoea, pulmonary oedema, dependent oedema, cardiomegaly and hepatomegaly, oliguria, ascites, pleural effusion, and gallop rhythm.

Life-threatening CHF is the most severe form of anthracycline -induced cardiomyopathy and represents the cumulative dose-limiting toxicity of the drug.

The risk of developing CHF increases rapidly with increasing total cumulative doses of epirubicin in excess of 900 mg/m^2; this cumulative dose should only be exceeded with extreme caution.

Cardiac function should be assessed before patients undergo treatment with epirubicin and must be monitored throughout therapy to minimize the risk of incurring severe cardiac impairment. The risk may be decreased through regular monitoring of LVEF during the course of treatment with prompt discontinuation of epirubicin at the first sign of impaired function.

The appropriate quantitative method for repeated assessment of cardiac function (evaluation of LVEF) includes multi-gated radionuclide angiography (MUGA) or echocardiography (ECHO). A baseline cardiac evaluation with an ECG and either a MUGA scan or an ECHO is recommended, especially in patients with risk factors for increased cardiotoxicity. Repeated MUGA or ECHO determinations of LVEF should be performed, particularly with higher, cumulative anthracycline doses. The technique used for assessment should be consistent throughout follow-up. Given the risk of cardiomyopathy, a cumulative dose of 900 mg/m^2 epirubicin should be exceeded only with extreme caution.

Risk factors for cardiac toxicity include active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, and concomitant use of other drugs with the ability to suppress cardiac contractility or cardiotoxic drugs (e.g., trastuzumab).

Cardiac function monitoring must be particularly strict in patients receiving high cumulative doses and in those with risk factors. However, cardiotoxicity with epirubicin may occur at lower cumulative doses whether or not cardiac risk factors are present. It is probable that the toxicity of epirubicin and other anthracyclines or anthracenediones is additive.

Haematologic Toxicity- As with other cytotoxic agents, epirubicin may produce myelosuppression. Haematologic profiles should be assessed before and during each cycle of therapy with epirubicin, including differential white blood cell (WBC) counts. A dose-dependent, reversible leucopoenia and/or granulocytopenia (neutropenia) is the predominant manifestation of epirubicin haematologic toxicity and is the most common acute dose-limiting toxicity of this drug. Leucopoenia and neutropenia are generally more severe with high-dose schedules, reaching the nadir in most cases between days 10 and 14 after drug administration; this is usually transient with the WBC/neutrophil counts returning to normal values in most cases by day 21. Thrombocytopenia and anaemia may also occur. Clinical consequences of severe myelosuppression include fever, infection, sepsis/septicaemia, septic shock, haemorrhage, tissue hypoxia, or death.

Secondary Leukaemia - Secondary leukaemia, with or without a preleukaemic phase, has been reported in patients treated with anthracyclines, including epirubicin.

Secondary leukaemia is more common when such drugs are given in combination with DNA-damaging antineoplastic agents, in combination with radiation treatment, when patients have been heavily pre-treated with cytotoxic drugs, or when doses of the anthracyclines have been escalated. These leukaemia's can have a 1- to 3-year latency period.

Gastrointestinal - Epirubicin is emetigenic. Mucositis/ stomatitis generally appears early after drug administration and, if severe, may progress over a few days to mucosal ulcerations. Most patients recover from this adverse event by the third week of therapy.

Liver Function - The major route of elimination of epirubicin is the hepatobiliary system. Serum total bilirubin and AST levels should be evaluated before and during treatment with epirubicin. Patients with elevated bilirubin or AST may experience slower clearance of drug with an increase in overall toxicity. Lower doses are recommended in these patients. Patients with severe hepatic impairment should not receive epirubicin.

Renal Function - Serum creatinine should be assessed before and during therapy. Dosage adjustment is necessary in patients with serum creatinine > 5 mg/dL.

Effects at Site of Injection - Phlebosclerosis may result from an injection into a small vessel or from repeated injections into the same vein. Following the recommended administration procedures may minimize the risk of phlebitis/thrombophlebitis at the injection site.

Extravasation- Extravasation of epirubicin during intravenous injection may produce local pain, severe tissue lesions (vesication, severe cellulitis) and necrosis. Should signs or symptoms of extravasation occur during intravenous administration of epirubicin, the drug infusion should be immediately discontinued. The patient's pain may be relieved by cooling down the area and keeping it cool for 24 hours. The patient should be monitored closely during the subsequent period of time, as necrosis may occur after several weeks extravasation occurs, a plastic surgeon should be consulted with a view to possible excision.

Other - As with other cytotoxic agents, thrombophlebitis and thromboembolic phenomena, including pulmonary embolism (in some cases fatal), have been coincidentally reported with the use of epirubicin

Tumor-Lysis Syndrome - Epirubicin may induce hyperuricemia because of the extensive purine catabolism that accompanies rapid drug-induced lysis of neoplastic cells (tumour-lysis syndrome). Blood uric acid levels, potassium, calcium phosphate, and creatinine should be evaluated after initial treatment. Hydration, urine alkalinization, and prophylaxis with allopurinol to prevent hyperuricemia may minimize potential complications of tumour-lysis syndrome.

Immunosuppressant Effects/Increased Susceptibility to Infections- Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including epirubicin, may result in serious or fatal infections.

Reproductive system: Epirubicin can cause genotoxicity. Men and women treated with epirubicin should adopt appropriate contraceptives Patients desiring to have children after completion of therapy should be advised to obtain genetic counselling if appropriate and available.

Pregnancy and Lactation

Impairment of Fertility

Epirubicin could induce chromosomal damage in human spermatozoa. Men undergoing treatment with epirubicin should use effective contraceptive methods and if appropriate and available, seek advice on sperm preservation due to the possibility of irreversible infertility caused by therapy. Epirubicin may cause amenorrhea or premature menopause in premenopausal women.

Pregnancy

Experimental data in animals suggest that epirubicin may cause fetal harm when administered to a pregnant woman. If epirubicin is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

There are no studies in pregnant women. Epirubicin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

It is unknown whether epirubicin is excreted in human breast milk. Because many drugs, including other anthracyclines, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from epirubicin, mothers should discontinue nursing prior to taking this drug.

ADVERSE REACTIONS

The estimation of frequency: Very common (≥ 1/10); common (≥ 1/100, <1/10); uncommon (≥ 1/1,000, <1/100); rare (≥ 1/10,000, <1/1,000); very rare (<1/10,000) not known (cannot be estimated from the available data).

The most common undesirable effects are myelosuppression, gastrointestinal side effects, anorexia, alopecia, infection.

Infections and infestations

Common: Infections

Not known: pneumonia, sepsis and septic shock may occur as a result of myelosuppression.

Neoplasms benign, malignant and unspecified (including cysts and polyps)

Rare: Acute lymphocytic leukaemia, Secondary acute myeloid leukaemia with or without a pre-leukaemic phase in patients treated with epirubicin in combination with DNA-damaging antineoplastic agents. These leukaemia's have short (1-3 years) latency.

Blood and lymphatic system disorder

Very common: Myelosuppression* (leukopenia, granulocytopenia and neutropenia, anaemia and febrile neutropenia).

Uncommon: Thrombocytopenia.

Not known: Haemorrhage and tissue hypoxia as result of myelosuppression.

* High doses of epirubicin have been safely administered in a large number of untreated patients having various solid tumours and have caused adverse events which are no different from those seen at conventional doses with the exception of reversible severe neutropenia (< 500 neutrophils /mm^3 for < 7 days) which occurred in the majority of patients. Only few patients required hospitalisation and supportive therapy for severe infectious complications at high doses.

Immune system disorders

Rare: Anaphylaxis.

Metabolism and nutrition disorders

Common: Anorexia, dehydration.

Rare: Hyperuricaemia (as a result of rapid lysis of neoplastic cells)

Nervous system disorders

Rare: Dizziness

Eye disorders

Not known: Conjunctivitis, keratitis

Cardiac disorders

Rare: Cardiotoxicity (ECG changes, tachycardia, arrhythmia, cardiomyopathy, congestive heart failure (dyspnoea, oedemea, enlargement of the liver, ascites, pulmonary oedema, pleural effusion, gallop rythm), ventricular tachycardia, bradycardia, AV block, bundle-branch block)

Vascular disorders

Common: Hot flushes.

Uncommon: Phlebitis, Thrombophlebitis.

Not known: Shock, Coincidental cases of thromboembolic events (including pulmonary embolism (in isolated cases with fatal outcome)) have occurred.

Gastrointestinal disorders

Common: Mucositis may appear 5-10 days after the start of treatment and usually involves stomatitis with areas of painful erosions, ulceration and bleedings, mainly along the side of the tongue and the sublingual mucosa, esophagitis, vomiting, diarrhoea, nausea

Skin and subcutaneous tissue disorders

Very Common: Alopecia

Rare: Urticaria

Not Known: Local toxicity, rash, itch, skin changes, erythema, flushes, skin and nail hyperpigmentation, photosensitivity, hypersensitivity to irradiated skin (radiation-recall reaction)

Renal and urinary disorders

Very common: Red coloration of urine for 1 to 2 days after administration

Reproductive system and breast disorders

Rare: Amenorrhea, azoospermia.

General disorders and administration site conditions

Common: Redness along the infusion vein. Phlebosclerosis, Local pain and tissue necrosis may occur (following accidental paravenous injection).

Rare: Fever, chills, hyperpyrexia, malaise, asthenia, weakness.

Investigations

Rare: Increased transaminase levels.

Not Known: Asymptomatic drops in left ventricular ejection fraction

DRUG INTERACTIONS

Epirubicin is mainly used in combination with other anti-cancer agents. Additive toxicity may occur especially with regard to bone marrow/hematologic and gastrointestinal effects. The use of epirubicin in combination chemotherapy with other potentially cardiotoxic drugs, as well as the concomitant use of other cardioactive compounds (e.g., calcium channel blockers), requires monitoring of cardiac function throughout treatment.

Epirubicin is extensively metabolized by the liver. Changes in hepatic function induced by concomitant therapies may affect epirubicin metabolism, pharmacokinetics, therapeutic efficacy and/or toxicity.

Anthracyclines including epirubicin should not be administered in combination with other cardiotoxic agents unless the patient's cardiac function is closely monitored. Patients receiving anthracyclines after stopping treatment with other cardiotoxic agents, especially those with long half-lives such as trastuzumab, may also be at an increased risk of developing cardiotoxicity. The half-life of trastuzumab is approximately 28.5 days and may persist in the circulation for up to 24 weeks.

Therefore, physicians should avoid anthracycline - based therapy for up to 24 weeks after stopping trastuzumab when possible. If anthracyclines are used before this time, careful monitoring of cardiac function is recommended.

Vaccination with a live vaccine should be avoided in patients receiving epirubicin. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

Cimetidine 400 mg b.i.d given prior to epirubicin 100 mg/m2 every 3 weeks led to a 50% increase in epirubicin AUC and a 41% increase in epirubicinol AUC (latter p<0.05). The AUC of the 7-deoxy-doxorubicinol aglycone and liver blood flow were not reduced, so results are not explained by reduced cytochrome P-450 activity. Epirubicin used in combination with other cytotoxic agents may result in additive myelotoxicity.

When given prior to epirubicin, paclitaxel can cause increased plasma concentrations of unchanged epirubicin and its metabolites, the latter being, however, neither toxic nor active. Coadministration of paclitaxel or docetaxel did not affect the pharmacokinetics of epirubicin when epirubicin was administered prior to the taxane.

This combination may be used if using staggered administration between the two agents. Infusion of epirubicin and paclitaxel should be performed with at least a 24 hour interval between the 2 agents.

Dexverapamil may alter the pharmacokinetics of epirubicin and possibly increase its bone marrow depressant effects.

One study found that docetaxel may increase the plasma concentrations of epirubicin metabolites, when administered immediately after epirubicin.

Quinine may accelerate the initial distribution of epirubicin from blood in to the tissues and may have an influence on the red blood cells partitioning of epirubicin.

The co-administration of interferon α2b may cause a reduction in both the terminal elimination half-life and the total clearance of epirubicin. The possibility of a marked disturbance of haematopiesis needs to be kept in mind with a (pre-) treatment with agents which influence the bone marrow (i.e. cytostatic agents, sulphonamide, chloramphenicol, diphenylhydantoin, amidopyrinederivatives, antiretroviral agents)

OVERDOSAGE

Acute overdosage with epirubicin will result in severe myelosuppression (mainly leukopenia and thrombocytopenia), gastrointestinal toxic effects (mainly mucositis) and acute cardiac complications. Latent cardiac failure has been observed with anthracyclines several months to years after completion of treatment. Patients must be carefully monitored. If signs of cardiac failure occur, patients should be treated according to conventional guidelines.

Treatment:

Symptomatic: Treatment should aim to support the patient during this period and should utilise such measures as blood transfusion and reverse barrier nursing.Delayed cardiac failure has been seen with the anthracyclines up to 6 months after the overdose. Patients should be observed carefully and should, if signs of cardiac failure arise, be treated along conventional lines. Epirubicin is not dialyzable

Expiry Date:

Do not use later than the date of expiry.

STORAGE

Store between 15^{0}C and 30^{0}C. Protect from light and moisture. Keep out of reach of children

PRESENTATION

TORRENCE (Epirubicin Hydrochloride for Injection) is available as sterile single dose lyophilised Injection in a vial containing Epirubicin Hydrochloride B.P. 10 mg/vial and 50mg/vial.

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured by :
Naprod Life Sciences Pvt. Ltd.
G-17/1, M.I.D.C.,Tarapur Industrial Area, Boisar,
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