Dobixin

Doxorubicin Hydrochloride USP 10mg & 50mg Injection

Composition :

Dobixin- 10: Each vial (5 ml) contains Doxorubicin Hydrochloride USP 10 mg Sterile Injectable Solution for Intravenous use.

Dobixin- 50: Each vial (25 ml) contains Doxorubicin Hydrochloride USP 50 mg Sterile Injectable Solution for Intravenous use.

Description :

Doxorubicin is a cytotoxic anthracycline antibiotic isolated from *Streptomyces peucetius* var. caesius. Doxorubicin, which is the established name for (8S,10S)-10-[(3-amino-2,3,6- trideoxy-α-L-lyxo-hexopyranosyl)oxy]-8-glycolyl-7,8,9,10-tetrahydro-6,8,11 trihydroxy-1-methoxy-5,12 naphthacenedione hydrochloride. The molecular formula of the drug is C_{27} H_{29} NO_{11}·HCl; its molecular weight is 579.99.

Mechanism of action :

The cytotoxic effect of Doxorubicin on malignant cells and its toxic effects on various organs are thought to be related to nucleotide base intercalation and cell membrane lipid binding activities of Doxorubicin. Intercalation inhibits nucleotide replication and action of DNA and RNA polymerases. The interaction of Doxorubicin with topoisomerase II to form DNA cleavable complexes appears to be an important mechanism of Doxorubicin cytocidal activity.

Doxorubicin cellular membrane binding may affect a variety of cellular functions. Enzymatic electron reduction of Doxorubicin by a variety of oxidases, reductases and dehydrogenases generates highly reactive species including the hydroxyl free radical OHo. Free radical formation has been implicated in Doxorubicin cardiotoxicity by means of Cu (II) and Fe (III) reduction at the cellular level.

Cells treated with Doxorubicin have been shown to manifest the characteristic morphologic changes associated with apoptosis or programmed cell death. Doxorubicin-induced apoptosis may be an integral component of the cellular mechanism of action relating to therapeutic effects, toxicities, or both.

Indications :

It is indicated for the treatment of acute lymphoblastic & myeloblastic leukemia, Hodgkin & non-Hodgkin lymphoma (NHL), metastatic breast cancer, metastatic Wilms' tumor, metastatic neuroblastoma, metastatic soft tissue sarcoma, metastatic bone sarcoma, metastatic ovarian carcinoma, metastatic transitional cell bladder carcinoma, metastatic thyroid carcinoma, metastatic gastric carcinoma & metastatic bronchogenic carcinoma.

Dosage and administration:

Adjuvant Breast Cancer

The recommended dose is 60 mg/m^2 administered as an intravenous bolus on day 1 of each 21-day treatment cycle, in combination with cyclophosphamide, for a total of four cycles.

Metastatic Disease, Leukemia, or **Lymphoma**

i) The recommended dose of Doxorubicin HCl when used as a single agent is 60 to 75 mg/m^2 intravenously every 21 days.

ii) The recommended dose when administered in combination with other chemotherapy drugs, is 40 to 75 mg/m^2 intravenously every 21 to 28 days.

iii) Consider use of the lower Doxorubicin dose in the recommended dose range or longer intervals between cycles for heavily pretreated patients, elderly patients, or obese patients. iv) Cumulative doses above 550 mg/m^2 are associated with an increased risk of cardiomyopathy.

It is recommended that Doxorubicin be slowly administered into the tubing of a freely running intavenous infusion of Sodium Chloride injection, USP, or 5% Dextrose injection, USP. The tubing should be attached to a Butterfly needle inserted preferably into a large vein. If possible, avoid veins over joints or in extremities with compromised venous or lymphatic drainage. The rate of administration is dependent on the size of the vein, and the dosage. However, the dose should be administered in not less than 3 to 5 minutes. Or, as directed by the registered physicians.

Dose Modifications :

Cardiac Impairment

Discontinue Doxorubicin in patients who develop signs or symptoms of cardiomyopathy.

Hepatic Impairment

Doxorubicin HCl is contraindicated in patients with severe hepatic impairment.

Decrease the dose of Doxorubicin HCl in patients with elevated serum total bilirubin concentrations as follows:

Serum bilirubin concentration	Doxorubicin HCl Dose reduction
1.2 - 3.0 mg/dL	50 %
3.1 - 5.0 mg/dL	75 %
greater than 5.0 mg/dL	Do not initiate Doxorubicin HCl Discontinue Doxorubicin HCl

Side effects :

Adverse reactions are: cardiotoxicity, acute nausea & vomiting, myelosuppression, thrombocytopenia, anemia, anaphylaxis, seizures & coma.

Contraindication :

Patients should not be treated with Doxorubicin if they have any of the following conditions: baseline neutrophil count <1500 cells/mm^3; severe hepatic impairment; recent myocardial infarction; severe myocardial insufficiency; severe arrhythmias; previous treatment with complete cumulative doses of Doxorubicin, Daunorubicin, Idarubicin, and/or other anthracyclines and anthracenediones; or hypersensitivity to Doxorubicin, any of its excipients, or other anthracyclines or anthracenediones.

Drug interactions :

Cyclosporine may induce coma and/or seizures, Phenobarbital increases the elimination of Doxorubicin, Phenytoin levels may be decreased by Doxorubicin, Streptozocin may inhibit the hepatic metabolism, and administration of live vaccines to immunosuppressed patients, including those undergoing cytotoxic chemotherapy, may be hazardous.

Precautions :

Doxorubicin is not an anti-microbial agent. It is emetigenic. Antiemetics may reduce nausea and vomiting; prophylactic use of antiemetics should be considered before administration of Doxorubicin, particularly when given in conjunction with other emetigenic drugs.

Use in pregnancy and lactation :

Pregnancy Category D. There are no adequate and well-controlled studies in pregnant women. If Doxorubicin is to be used during pregnancy, or if the patient becomes pregnant during therapy, the patient should be apprised of the potential hazard to the fetus. Women of childbearing age should be advised to avoid becoming pregnant.

Overdose :

Acute overdosage with Doxorubicin enhances the toxic effect of mucositis, leukopenia and thrombocytopenia. Cumulative dosage with Doxorubicin increases the risk of cardiomyopathy and cause congestive heart failure.

Storage :

Store at 2°- 8° C in a dry place.

Packing :

Dobixin- 10: Each box contains one vial of Doxorubicin Hydrochloride USP 10 mg Sterile Solution.

Dobixin- 50: Each box contains one vial of Doxorubicin Hydrochloride USP 50 mg Sterile Solution.

DRUG INTERNATIONAL LTD.
UNIT-2
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