

INJECTION  
**D-BLASTIN 20mg**  
**U.S.P Specs.**  
**(DAUNORUBICIN HCl U.S.P)**

انجشٹن  
**ڈی بلاسٹن 20 ملی گرام**  
(ڈاؤنوروبین ہائیدروکلورائیڈ) یو۔س۔پ

**Action And Clinical Pharmacology:** Daunorubicin inhibits the synthesis of nucleic acids; its effect on deoxyribonucleic acid is particularly rapid and marked. Ribonucleic acid is more gradually affected. It appears that the action of the drug is the result of the formation of a complex with deoxyribonucleic acid in the cell nucleus; this blocks the site of action of the polymerases and gives daunorubicin a cytostatic activity. Daunorubicin displays an immunosuppressive action. Daunorubicin has no effect on respiration or cellular glycolysis up to elevated concentrations which would inhibit cell growth. It exerts an antiviral effect on the herpes and on the vaccine viruses of the deoxyribonucleic acid group, but not on the polio or influenza virus of the ribonucleic acid group. Daunorubicin is inactive when administered orally.

**Teratogenicity:** Teratogenic effects have not been observed in the chicken embryo, even at embryotoxic doses. In the mouse, prolonged treatment at a dose of 1.15 mg/kg s.c. daily did not interfere with gestation or produce any teratogenic effects.

In rabbits, doses of 90 µg/kg and 250 µg/kg i.v. induced 66% and 100% abortions respectively; in some fetuses, abnormalities which could not be attributed to the drug, were observed.

**Indications and Clinical Uses:** The initial treatment of myeloblastic and acute lymphoblastic leukemias. Daunorubicin can also induce a remission in patients suffering from chronic myeloid leukemia, reticulosarcomas, Ewing or Wilms' tumors and lymphosarcoma.

**Precautions:** Daunorubicin induces medullary aplasia and leukopenia. It is therefore imperative that patients be protected against infection during the period of aplasia.

At the start of therapy, the increase in uric acid in the blood due to leukocyte degradation can be controlled by administering allopurinol and liquids to stimulate urine excretion. Caution must be exercised in patients with renal insufficiency. Daunorubicin can cause tissue necrosis, thus great care must be taken to inject the product directly into the vein. When daunorubicin is employed in association with other anticancer agents, the dosage of each should be reduced so as to minimize the total toxic effect.

Some instances of cardiotoxicity may be observed when a cumulative dose of 25 mg/kg has been reached; in general, this dose must not be exceeded except in certain desperate cases where 30 mg/kg can be administered. Likewise, because of possible cardiotoxicity, the drug must not be administered to patients who exhibit myocardial lesions or to those 75 years of age. Before initiating treatment with daunorubicin, physical examination, appropriate x-rays and ECG should be performed and repeated at regular intervals thereafter, particularly when the cumulative dose has reached 15 mg/kg.

Daunorubicin should be employed only as a treatment to induce a remission, and not as maintenance therapy.

**Adverse Reactions:** At the start of treatment, the patient may experience anorexia, nausea and vomiting. These are transient effects and generally do not require an interruption of treatment. Antiemetics may help relieve vomiting.

Abdominal pain, constipation or diarrhea, alopecia, rash, petechiae or purpura may be observed during therapy. Some cases of thrombocytopenia and anemia have been reported during the first or second week of treatment. These phenomena are transient and corrective measures such as blood or platelet transfusions are rarely required. During the aplastic phase, cases of localized infection have occurred, particularly in the buccal cavity or pharynx. Septicemia not responsive to antibiotics has also been reported. Some cases of cardiopathy attended by rhythm abnormalities, electrical modifications and indications of cardiac

insufficiency have been observed in patients receiving a cumulative dose exceeding 30 mg/kg.

In young patients, the urine occasionally acquires a red tint. This coloration is due to the presence of daunorubicin and its metabolites and has no clinical significance. During treatment with combinations of daunorubicin with other antileukemic agents, there have been occurrences of myalgia and neuropathy. These symptoms, already associated with the use of other agents, have not been directly attributed to daunorubicin.

**Dosage and Administration:** Daunorubicin is reserved mainly for the initial therapy of acute leukemia and other forms of malignant tumors which are sensitive to the drug. It is administered by the i.v. route only. After dilution in 4 mL of sterile water for injection, daunorubicin is injected into the tubing of a running infusion of 100 or 250 mL of isotonic solution. The infusion is performed rapidly to avoid local stasis.

Freshly prepared solution may be kept for a period of 24 hours at room temperature or 48 hours in a refrigerator.

**Initial treatment: A) Daunorubicin Alone:** acute Lymphoblastic Leukemia: Daunorubicin is instituted at a daily dose of 1 mg/kg (30 mg/m<sup>2</sup> over a period of from 3 to 6 days. If, after this first administration, the number of white cells is less than 1500, maintenance therapy is begun. However, if a partial remission is obtained, but the number of leukocytes is greater than 1500, treatment should be repeated 1 or more times, as necessary, based on the hematologic response. As soon as the remission is obtained, maintenance treatment can be started. The total dose during the initial treatment should not, as a rule, exceed 20 mg/kg.

The dosage is from 1 mg/kg per injection every 2 or 3 days up to a total of 12 mg/kg. If only an incomplete remission is obtained after this treatment, daunorubicin can be continued up to the maximum dose of 20 mg/kg which must not be exceeded during any one treatment period. As soon as a complete remission is obtained the drug is withdrawn and maintenance treatment instituted.

**Maintenance Treatment:** Any standard chemotherapeutic agent may be employed during maintenance therapy. If the marrow is not completely ablastic in the course of 4 weeks, a weekly injection of 1 mg/kg daunorubicin may be given.

**Cumulative Doses:** As a rule the total cumulative dose should not exceed 25 mg/kg, e.g., approximately 500 mg/m<sup>2</sup> for a child of 10 kg; 600 mg/m<sup>2</sup> for child of 20 kg; 750 mg/m<sup>2</sup> for a child of 30 kg and 900 mg/m<sup>2</sup> for an adult of 60 kg. In patients who have become resistant to all therapy and for whom a final effort is required to induce a remission, the total cumulative dose can be extended to 30 mg/kg.

**Chronic Myeloid Leukemia: Injections of 1 to 2 mg/kg may be administered**

**Chronic Myeloid Leukemia:** Injections of 1 to 2 mg/kg may be administered every other day up to a total dose of 6 to 12 mg/kg.

**Availability And Storage:** Each vial contains; sterile Daunorubicin Hydrochloride U.S.P. equivalent to Daunorubicin 20mg. Box of 1vial.

**Nonmedicinal ingredients:** D-mannitol in dry powder form with ampoule of 5ml of sterile water for injection as solvent.

**Dosage:** As directed by the physician.

**Instructions:** Store below 25 °C. Protect from heat, light and moisture. Keep all medicines out of the reach of children. To be sold on prescription of registered medical practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایت: 25 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، نمی اور روشنی سے بچائیں۔

تھام ادویات بچوں کی پہنچ سے دور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

Manufactured by:

**PHARMEDIC LABORATORIES (PVT) LIMITED.**

16 Km. Multan Road, Lahore - Pakistan