DaunoXome®
(daunorubicin liposome injection)

**INDICATIONS AND USAGE**

DaunoXome is indicated for the treatment of patients with Kaposi’s sarcoma and advanced HIV-associated Kaposi’s sarcoma. DaunoXome is intended for administration under the supervision of a physician who is experienced in the use of cancer chemotherapy agents.

**CONTRAINDICATIONS**

DaunoXome is contraindicated in patients who have experienced a serious hypersensitivity reaction to daunorubicin or any of the components of DaunoXome, or who are hypersensitive to any other anthracycline.

**WARNINGS**

Cardiac function should be evaluated regularly in patients treated with DaunoXome. Drug-induced cardiomyopathy or life-threatening cardiotoxicity is a rare event associated with anthracyclines. Cardiac function should be evaluated before starting DaunoXome and prior to each subsequent course of DaunoXome. Cardiac function should be assessed by a history, physical examination, and measurement of left ventricular ejection fraction (LVEF) prior to starting this therapy, and at regular intervals thereafter. DaunoXome should be administered under the supervision of a physician who is experienced in the use of cancer chemotherapy agents.

**ADVERSE REACTIONS**

DaunoXome is a liposomal formulation of daunorubicin designed to minimize protein binding, and generally decreases uptake and clearance of daunorubicin. These changes in the pharmacokinetics of daunorubicin can result in differences in pharmacodynamic activity. These differences can be attributed to the liposomal encapsulation of daunorubicin.

**PHARMACOKINETICS**

The pharmacokinetic profile of DaunoXome (daunorubicin citrate liposome injection) is 4-6 hours shorter than that of daunorubicin hydrochloride. Since daunorubicin is an active component of the liposomes in DaunoXome, it is released from the liposome to become available for pharmacodynamic activity.

**DRUG INTERACTIONS**

DaunoXome is not a substrate, inducer, or inhibitor of CYP3A4. DaunoXome is not a P-glycoprotein substrate. DaunoXome does not affect the metabolism of substrates of CYP3A4, P-glycoprotein, or OAT1/3,2,1 (OATP1B1). DaunoXome may affect the metabolism of substrates of CYP2C9.

**PREGNANCY CATEGORY D**

DaunoXome may cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be warned of the potential hazard to the fetus. DaunoXome is contraindicated in women who are pregnant.

**NURSING MOTHERS**

It is unknown whether DaunoXome is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

**DOSE AND ADMINISTRATION**

DaunoXome may be administered in a single 30 mg/m² dose every 21 days for 6 cycles, as a 30 minute intravenous infusion, according to the protocol used in the randomized clinical trial. DaunoXome may be used in the following regimens:

- 1.0 mg/m² of DaunoXome every 3 weeks, according to the protocol used in the randomized clinical trial.
- 40 mg/m² of DaunoXome every 21 days, according to the protocol used in the randomized clinical trial.

**CONVIVIENTAL OUTCOME PARAMETERS**

In a randomized clinical trial, patients treated with DaunoXome in the 30 mg/m² dose had a median duration of response of 113 days. The hazard ratio (ABV/DaunoXome) was 2.05 (95% confidence interval, 1.15 to 3.64; p = 0.0114). The median duration of response in patients treated with DaunoXome in the 40 mg/m² dose was 110 days. The hazard ratio (ABV/DaunoXome) was 2.06 (95% confidence interval, 1.15 to 3.67; p = 0.0112). The median duration of response in patients treated with DaunoXome in the 1.0 mg/m² dose was 104 days. The hazard ratio (ABV/DaunoXome) was 1.85 (95% confidence interval, 1.03 to 3.31; p = 0.0371).

**ADVERSE REACTIONS**

DaunoXome is associated with a high likelihood of antitumor activity. DaunoXome is also associated with a high likelihood of adverse events. DaunoXome is associated with a high likelihood of hematologic toxicity. DaunoXome is associated with a high likelihood of cardiotoxicity. DaunoXome is associated with a high likelihood of non-hematologic toxicities. DaunoXome is associated with a high likelihood of drug interactions. DaunoXome is associated with a high likelihood of pregnancy consequences. DaunoXome is associated with a high likelihood of nursing consequences.

**BIBLIOGRAPHY**

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Table III summarizes the important safety data.

Table IV is a listing of all the mild-moderate and severe adverse experiences reported in patients treated with DaunoXome. Details of the most important adverse experiences are given below.

Adverse reactions were recorded as follows:
- **Mild**: grade 1 (≥5% to <10% of patients treated)
- **Moderate**: grade 2 (≥5% to <10% of patients treated)
- **Severe**: grade 3 (≥1% to <5% of patients treated)
- **Very Severe**: grade 4 (≥1% to <5% of patients treated)

**Gastrointestinal:**
- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Dyspepsia
- Edema
- Fever
- Influenza-like symptoms
- Stomatitis
- Tenesmus
- Hemorrhage

**Hematological:**
- Leukopenia
- Neutropenia
- Febrile neutropenia
- Thrombocytopenia
- Anemia
- Thrombocytosis

**Cardiovascular:**
- Hypertension
- Hypotension
- Palpitations
- Arrhythmia
- Chest pain
- Shortness of breath
- Effusion
- Pericardial tamponade
- Ventricular extrasystoles
- Cardiomyopathy
- Congestive heart failure

**Central Nervous System:**
- Numbness
- Taste perversion
- Tinnitus
- Somnolence
- Abnormal thinking
- Tremor
- Hyperkinesia
- Hypertonia
- Meningitis
- Increased sputum

**Other Adverse Reactions:**
- Alopecia
- Increased sweating
- Back pain
- Headache
- Fatigue
- Myalgia
- Arthralgia
- Increased thirst
- Gastrointestinal intolerance
- Cough
- Rash, pruritus
- Edema, fluid retention
- Palmar-plantar erythrodysesthesia
- Direct manual compression
- Indirect manual compression
- Local discomfort
- Hemorrhage

**Other Local Reactions:**
- Injection site pain
- Injection site tenderness
- Injection site hematoma
- Increased pain at the injection site

**Other Events:**
- Increased appetite
- Dysphagia
- GI hemorrhage
- Aspiration
- Cutaneous lesions
- Fever
- Influenza
- Rash
- Abnormal taste
- Growth of hair

**Special Populations:**
- **Pediatric Patients:**
  - Safety and effectiveness in pediatric patients have not been established.
- **Pregnancy:**
  - **Category D**
- **Lactation:**
  - Breastfeeding is not recommended.

**Precautions:**
- **Hematologic:**
  - Monitor hematologic parameters and blood counts during therapy.
- **Renal Function:**
  - Reduce the dose in patients with severe renal impairment.
- **Hepatic Function:**
  - Consider dose reduction in patients with severe hepatic impairment.

**Adverse Reactions with Other Drugs:**
- **Intravenous Drug Administration:**
  - DaunoXome should be administered separately from other intravenous drugs.
- **Oral Drug Administration:**
  - DaunoXome should not be administered with oral drugs.

**DOSAGE AND ADMINISTRATION:**
- **Adults:** 50 mg of daunorubicin base, at a concentration of 2 mg/mL.
- **Children:** 50 mg of daunorubicin base, at a concentration of 2 mg/mL.
- **Dilution:** The recommended concentration after dilution is 1 mg/mL.

**Storage:**
- Store DaunoXome in a refrigerator, 2°-8°C (36°-46°F).

**References:**