DOXIL® (doxorubicin hydrochloride liposome injection), for intravenous use

DOXIL® (doxorubicin hydrochloride liposome injection)

12.1 Doxorubicin Hydrochloride (HCl) Liposomal Injection

Doxorubicin hydrochloride (HCl) liposomal injection: Single use vials: (doxorubicin hydrochloride liposome injection), 30 mg (10 mg/mL) and 50 mg (10 mg/mL).

13.1 Preparation and Administration

To ensure fluid and drug compatibility, DOXIL® is recommended for use in 5% dextrose injection or 0.9% sodium chloride injection.

16.6 Special Senses

Taste perversion, conjunctivitis.

16.10 Other Reactions

Dose modifications for adverse reactions are based on clinical judgment and may be required (5.3). Procedure for Proper Handling and Disposal

Ensure that medications to treat infusion-related reactions and cardiopulmonary toxicity are readily available during administration.

11.1 Pharmacology

Dose Adjustment

If the drug is administered overly quickly, the nurse should administer the remaining dose slowly. Recovery from the Dose Administration

In a clinical study in 250 patients with advanced cancer who were treated with DOXIL® (doxorubicin hydrochloride liposome injection), 15% of patients developed HFS. HFS in DOXIL-treated patients and no Grade 3 or 4 cases in topotecan-treated patients. [see Dosage and Administration (2.6)].

10.3.8 Patients With Ovarian Cancer

Hematologic Adverse Reactions

Table 5: Hematologic Adverse Reactions Reported in Patients With AIDS-Related Kaposi's Sarcoma

- 2.6 to 4.0 g/dL 3% 10%
- 1000 - <150,000/mm³ 4% 7%
- 500 - <1000/mm³ 8% 14%
- < 50/mm³ 1% 2%

10.3.6 Patients With Multiple Myeloma

Myocardial damage may lead to congestive heart failure and may occur even in the absence of cardiac symptoms. Cardiac symptoms include signs of fluid overload (eg, peripheral edema, weight gain, shortness of breath), palpitations and angina. If heart failure is suspected, re-evaluate the patient and consider DOXIL discontinuation: administration

Table 3: Non-Hematologic Adverse Reactions in Trial 3

Table 4: Non-Hematologic Adverse Reactions in Trial 4

1. Clinical Development

11.1 Pharmacology

- 10 g/dL 58% 55%
- 58% 55%

WARNING—CARDIOMYOPATHY and INFUSION-RELATED REACTIONS

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13.1 Preparation and Administration

To ensure fluid and drug compatibility, DOXIL® is recommended for use in 5% dextrose injection or 0.9% sodium chloride injection.

16.6 Special Senses

Taste perversion, conjunctivitis.
DOXIL® (doxorubicin hydrochloride liposome injection) is a fixed-dose combination product containing doxorubicin, an anthracycline topoisomerase II inhibitor, encapsulated in a polymeric matrix of glass, single-use vials. Each vial contains 20 mg or 50 mg doxorubicin HCl at 61% of the recommended dose of 50 mg/m² human dose on a mg/m² basis. DOXIL® is supplied in a glass, single-use vial. The active ingredient of DOXIL is doxorubicin HCl. The mechanism of action of DOXIL involves the delivery of doxorubicin by liposomes to tissues via an enhanced permeability and retention (EPR) effect. The liposomes are composed of a cationic polymer, polyethyleneimine, and a cationic lipid, cholesterol, which form a stable non-biodegradable complex. The carriers contain the doxorubicin HCl in a stealth liposomal formulation, which allows for sustained release of doxorubicin into the systemic circulation after infusion. The patient population in clinical studies with DOXIL included patients with advanced malignancies such as ovarian cancer, AIDS-related Kaposi’s sarcoma, and advanced malignancies resistant to chemotherapy. The response rate for patients with refractory ovarian cancer in phase III trials has been reported to be approximately 15-20%. The median time to progression has been reported to be 4-8 months, and the duration of response has been reported to be 10-20 months. DOXIL is contraindicated in patients who are hypersensitive to doxorubicin. It is also contraindicated in patients with known or suspected genitourinary malignancy. DOXIL is not recommended for use in patients with severe hepatic dysfunction or who are elderly. It is not recommended for use in women who are pregnant or breast-feeding. It is important to note that the administration of DOXIL should be performed under the supervision of a healthcare provider who is experienced in the use of chemotherapy agents.

**Mechanism of Action**

DOXIL is a liposomal formulation of doxorubicin designed to enhance the delivery of doxorubicin to tissues with enhanced permeability and retention (EPR) effect. The liposomes are composed of a cationic polymer, polyethyleneimine, and a cationic lipid, cholesterol, which form a stable non-biodegradable complex. The carriers contain doxorubicin HCl in a stealth liposomal formulation, which allows for sustained release of doxorubicin into the systemic circulation after infusion.

**Patient Population**

The patient population in clinical studies with DOXIL included patients with advanced malignancies such as ovarian cancer, AIDS-related Kaposi’s sarcoma, and advanced malignancies resistant to chemotherapy. The response rate for patients with refractory ovarian cancer in phase III trials has been reported to be approximately 15-20%. The median time to progression has been reported to be 4-8 months, and the duration of response has been reported to be 10-20 months.

**Contraindications**

DOXIL is contraindicated in patients who are hypersensitive to doxorubicin. It is also contraindicated in patients with known or suspected genitourinary malignancy. DOXIL is not recommended for use in patients with severe hepatic dysfunction or who are elderly. It is not recommended for use in women who are pregnant or breast-feeding. It is important to note that the administration of DOXIL should be performed under the supervision of a healthcare provider who is experienced in the use of chemotherapy agents.

**Warnings and Precautions**

- **Discoloration of Urine and Body Fluids**: A significant rate of temporary discoloration of urine and body fluids may occur during treatment with DOXIL due to the color of the product and will dissipate as the drug is eliminated. Therefore, it is recommended to use disposable materials or clean the area of discoloration. Patients should be instructed to use disposable hospital gowns or linens and to dispose of used linens properly.
- **Induction Hyperbilirubinemia**: As with other anthracyclines, DOXIL may result in an increased level of serum bilirubin. The increase in bilirubin levels usually occurs during the first 4 to 8 weeks of therapy but may occur at any time. The increase is generally asymptomatic and usually resolves when the drug is discontinued. The increase in serum bilirubin levels is not associated with an increase in the incidence of jaundice or hepatitis.
- **Hematologic Toxicity**: DOXIL may result in myelosuppression, which may be severe in some patients. The median time to nadir of white blood cell count (WBC) and platelets occurs approximately 14 days after dose administration. Neutropenic fever and sepsis have been reported to occur in some patients. Patients should be monitored for signs and symptoms of neutropenic fever and sepsis.
- **Tumor Lysis Syndrome (TLS)**: TLS may occur in patients with tumors that are rapidly metabolized such as acute leukemia or lymphoma. TLS is characterized by an increase in serum levels of uric acid, phosphate, and potassium. Patients with TLS may develop acute renal failure, electrolyte abnormalities, and cardiac arrhythmias. TLS may be prevented by the use of hydration, alkalinization of the urine, and the use of febuxostat or allopurinol.
- **Cardiomyopathy**: DOXIL may result in cardiomyopathy, which may be asymptomatic or progressive. The median time to the onset of cardiomyopathy occurs approximately 3 months after the start of therapy. Cardiomyopathy may be treated with diuretics, beta-blockers, and occasionally with angiotensin-converting enzyme (ACE) inhibitors. The use of DOXIL in patients with pre-existing cardiac disease should be approached with caution.
- **Acute Overdosage**: Acute overdosage with doxorubicin HCl causes increased risk of severe cardiac toxicity. The risk of cardiac toxicity increases with the cumulative dose of doxorubicin. In case of acute overdosage, supportive care and management of symptoms should be provided.

**Additional Information**

DOXIL is a registered trademark of GlaxoSmithKline Inc.
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