DOXorubicin, liposomal (dox-oh-roe-ly-som-al) Oral

**Classification**
- Therapeutic: antineoplastics
- Pharmacologic: anthracyclines

**Pregnancy Category** D

**Indications**
- AIDS-related Kaposi's sarcoma (KS) in patients who cannot tolerate or fail conventional therapy. Ovarian carcinoma. Multiple myeloma with bortezomib in patients who have not previously received bortezomib and have received at least one prior therapy.

**Action**
- Inhibits DNA and RNA synthesis by forming a complex with DNA; action is cell-cycle S-phase-specific. Also has immunosuppressive properties. Encapsulation in a liposome increases uptake by tumors, prolongs action, and may decrease some toxicity.

**Therapeutic Effects:** Death of rapidly replicating cells, particularly malignant ones.

**Pharmacokinetics**
- **Absorption:** Administered IV only, resulting in complete bioavailability.
- **Distribution:** Widely distributed; does not cross the blood-brain barrier; extensively bound to tissues (concentrations delivered to KS lesions due to liposomal carrier).
- **Metabolism and Excretion:** Mostly metabolized by the liver with conversion to an active compound. Excreted mostly in bile, 50% as unchanged drug. 5% eliminated unchanged in the urine.
- **Half-life:** 55 hr.

**TIME/ACTION PROFILE (effect on blood counts)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<tr>
<td>IV</td>
<td>10 days</td>
<td>14 days</td>
<td>21–24 days</td>
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**Contraindications/Precautions**
- Contraindicated in: Hypersensitivity; OR, Lactation: Pregnancy or lactation.

**Adverse Reactions/Side Effects**
- **CNS:** Weakness.
- **CV:** Cardiomyopathy.
- **GI:** Nausea, vomiting, alkaline phosphatase, moniliasis, or oral malignancy, stomatitis, vomiting.
- **Derm:** Alopecia, palmar-plantar erythrodysesthesia.
- **Hemat:** Anemia, leukopenia, thrombocytopenia.
- **Local:** Injection site reactions.
- **Misc:** Anaphylactic allergic reactions, fever.

**Interactions**
- **Drug-Drug:** Bone marrow depression with other antineoplastics or radiation therapy. Pediatric patients who have received concurrent doxorubicin and dactinomycin have risk of recall pneumonitis following local radiation therapy. May ↑ risk of infections following local radiation therapy. If paclitaxel is administered first, clearance of doxorubicin is ↑ and incidence and severity of neutropenia and stomatitis are ↑ (problems in use of doxorubicin in admixed form). Hematologic toxicity is ↓ in concurrent use of cyclosporine; risk of coma and seizures is also ↓. Incidence and severity of neutropenia and thrombocytopenia are ↑ in concurrent use of cyclosporine. Phlebitis is ↑ and clearance of doxorubicin. Doxorubicin may ↑ incidence of neutropenia and thrombocytopenia. Streptozocin may ↑ the half-life of doxorubicin (dose reduction of doxorubicin recommended). May ↑ antibody response to live-virus vaccines and ↑ risk of adverse reactions.

**Route/Dosage**
- Other regimens are used.
- **IV (Adults):** AIDS-related KS — 20 mg/m² every 3 wk; metastatic ovarian cancer — 40–50 mg/m² every 4 wk; multiple myeloma — 30 mg/m² on day 4 after following bortezomib for up to 8 cycles.
NURSING IMPLICATIONS

Assessment
- Monitor BP, pulse, respiration rate, and temperature frequently during administration. Report significant changes.
- Monitor for acute infusion-related reactions consisting of flushing, shortness of breath, facial swelling, headache, chill, chest pain, back pain, chest or throat tightness, fever, tachycardia, pruritis, rash, cyanosis, syncope, bronchoconstriction, nausea, apnea, which may be accompanied by hypotension. Infusions usually resolve over 1 day and are usually limited to first dose. Slowing infusion rate may minimize the reaction. Reaction is thought to be due to liposome.
- Monitor intake and output ratios, and report occurrence of significant discrepancies. Encourage fluid intake of 2000–3000 mL/day. Allopurinol and alkalization of the urine may be used to decrease serum uric acid levels and to help prevent urate stone formation.
- Monitor oral mucosa frequently for development of stomatitis. Increased dosing in infants, children, and geriatric patients. Dexrazoxane may be used to prevent cardiotoxicity in patients receiving cumulative doses of ≥ 800 mg/m².
- Monitor BP, pulse, respiration rate, and temperature frequently during administration. Report significant changes.
- Monitor for severe rash, pruritis, erythema, and urticaria. Avoid BM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture site for 10 min. Assess for signs of infection during neutropenia. Anemia may occur.
- Monitor for increased fatigue, dyspnea, and orthostatic hypotension.
- Monitor for bone marrow depression. Assess for bleeding (bleeding gums, petechiae, guaiac stools, urine, and emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture site for 10 min. Assess for signs of infection during neutropenia. Anemia may occur.
- Monitor for bone marrow depression. Assess for bleeding (bleeding gums, petechiae, guaiac stools, urine, and emesis) and avoid BM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture site for 10 min. Assess for signs of infection during neutropenia. Anemia may occur.
- Monitor for skin toxicity with prolonged use; palmar-plantar erythrodysesthesia may occur after 6 wk of treatment and consists of swelling, pain, and erythema of the hands and feet. This may progress to desquamation but usually regresses after several months.
- Monitor for increased intensity of rash. Increased dosing in children younger than 2 yr and geriatric patients. Dexrazoxane may be used to prevent cardiotoxicity in patients receiving cumulative doses of ≥ 800 mg/m².
- Monitor for acute infusion-related reactions consisting of flushing, shortness of breath, facial swelling, headache, chill, chest pain, back pain, chest or throat tightness, fever, tachycardia, pruritis, rash, cyanosis, syncope, bronchoconstriction, nausea, apnea, which may be accompanied by hypotension. Infusions usually resolve over 1 day and are usually limited to first dose. Slowing infusion rate may minimize the reaction. Reaction is thought to be due to liposome.
- Monitor for signs and symptoms of anaphylaxis (rash, pruritis, laryngeal edema, wheezing). Discontinue doxorubicin liposome and notify health care professional immediately if these problems occur. Keep epinephrine, an antihistamine, and resuscitation equipment close to in case of an anaphylactic reaction.
- Monitor for bone marrow depression. Assess for bleeding (bleeding gums, petechiae, guaiac stools, urine, and emesis) and avoid BM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture site for 10 min. Assess for signs of infection during neutropenia. Anemia may occur.
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CONTINUED

DOXOribucin, liposomal

(Grade 3, read until 3% doxorubicin - 15,000; then continue at 15%/day. reductions or complete drug with cyclophosphamide support)

INTERMITTENT INFUSION: Aluminum needles may be used to administer doxorubicin but should not be used for intermittent infusion. Prepare solution in a biologic cabinet. Wear gloves, gown, and mask while handling medication. Discard IV equipment in specially designated containers.

High Alert

INTERMITTENT INFUSION: Discontinue. Doxorubicin liposomal is not recommended for intravenous administration. Doxorubicin liposomal is for administration by direct intravenous injection. Use doxorubicin liposomal only at the start of a new treatment cycle. The starting dose for doxorubicin liposomal is 30 mg/m² administered as a single intravenous injection on days 1 and 8 of a 21-day cycle. Dose reductions or delays can be considered at the discretion of the treating physician. Dose reductions or delays should not be administered without consulting the prescribing physician.

IV Administration

Y-Site Compatibility: Do not confuse doxorubicin liposome (Doxil) with doxorubicin hydrochloride liposome (Cerubidine). Do not confuse Doxil with Paxil. Clarify orders that do not include generic and brand names. Direct pharmacological action of the lipoamide groups in doxorubicin liposomal inhibit DNA polymerase, RNA polymerase, and topoisomerase II, resulting in cell death.

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Patient/Family Teaching

- Instruct patient to notify health care professional promptly if fever; sore throat; signs of infection; bleeding gums; bruising; petechiae; blood in stools, urine, or emesis; increased fatigue; dyspnea; or respiratory hypoxia occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use soft toothbrush and electric razor and to avoid falls. Caution patient not to drink alcoholic beverages or take medications containing aspirin or NSAIDs; may precipitate gastric bleeding.

- Instruct patient to report pain at injection site immediately.

- Instruct patient to inspect oral mucosa for erythema and ulceration. If ulceration occurs, advise patient to use sponge brush, rinse mouth with water after eating and drinking, and confer with health care professional if mouth pain interferes with eating. Pain may require treatment with opioid analgesics. The risk of developing stomatitis is greatest 5–10 days after a dose; the usual duration is 1–7 days.

- Instruct patient to notify health care professional immediately if irregular heartbeat; shortness of breath; swelling of lower extremities; or skin irritation (swelling, pain, or redness of feet or hands) occurs.

- Discuss the possibility of hair loss with patient. Explore methods of coping. Regrowth usually occurs 2–3 mo after discontinuation of therapy.

- Instruct patient not to receive any vaccinations without advice of health care professional.

- Informs patient that medication may cause urine to appear red for 1–2 days.

- Instruct patient to notify health care professional if skin irritation occurs at site of previous radiation therapy.

- Advise family and/or caregivers to take precautions (i.e., latex gloves) in handling body fluids for at least 5 days posttreatment.

- Advise patient that this medication may cause irreversible gonadal suppression. Advise female patient to avoid breast feeding during therapy.

- Emphasize the need for periodic lab tests to monitor for side effects.

Evaluation/Desired Outcomes

- Decrease in size or spread of malignancies.

- Arrested progression of KS in patients with HIV infection.

Why was this drug prescribed for your patient?