Bleomycin:

Class: Antineoplastic Agent, Antibiotic

Indications: - Test dose for lymphoma patients - Hodgkin's lymphoma
- Testicular cancer - Ovarian germ cell cancer - Malignant pleural effusion

Available dosage form in the hospital: 15MG AMP

Trade Names: Bileco (AR); Blenamax (AU, RU, SG, TW); Blenoxane (BR, EC, EG, ZA); Bleo (HK); Bleocin

Dosage: Note: The risk for pulmonary toxicity increases with age >70 years and cumulative lifetime dose of >400 units; 1 unit = 1 mg. Details concerning dosage in combination regimens should also be consulted.

-**Test dose for lymphoma patients:** I.M., I.V., SubQ: Because of the possibility of an anaphylactoid reaction, the manufacturer recommends administering 1-2 units of bleomycin before the first 1-2 doses; monitor vital signs every 15 minutes; wait a minimum of 1 hour before administering remainder of dose; if no acute reaction occurs, then the regular dosage schedule may be followed. Note: Test doses may not be predictive of a reaction (Lam, 2005) and/or may produce false-negative results.

-**Hodgkin's lymphoma (unlabeled dosing; combination regimens):** I.V.:

-*ABVD:* 10 units/m^2 days 1 and 15 of a 28-day treatment cycle (Straus, 2004)

-*BEACOPP:* 10 units/m^2 day 8 of a 21-day treatment cycle (Dann, 2007; Diehl, 2003)

-*Stanford V:* 5 units/m^2/dose in weeks 2, 4, 6, 8, 10 and 12 (Horning, 2002; Horning, 2000)

-**Testicular cancer (unlabeled dosing; combination therapy):** I.V.: 30 units/dose days 1, 8, and 15 of a 21-day treatment cycle for 4 cycles (Culine, 2008; Nichols, 1998)

-**Ovarian germ cell cancer (unlabeled use; combination therapy):** I.V.: 30 units/dose days 1, 8, and 15 of a 21-day treatment cycle for 3 cycles (Williams, 1994) or 15 units/m^2 day 1 of a 21-day treatment cycle for 4 cycles (Cushing, 2004)

-**Malignant pleural effusion:** Intrapleural: 60 units as a single instillation; mix in 50-100 mL of NS

Geriatric
Refer to adult dosing. The incidence of pulmonary toxicity is higher in patients >70 years of age

Renal Impairment:
-The U.S. labeling recommends the following adjustments (creatinine clearance should be estimated using the Cockcroft-Gault formula):
- Cl_{cr} >50 mL/minute: No dosage adjustment necessary.
- Cl_{cr} 40-50 mL/minute: Administer 70% of normal dose
- Cl_{cr} 30-40 mL/minute: Administer 60% of normal dose
- Cl_{cr} 20-30 mL/minute: Administer 55% of normal dose
- Cl_{cr} 10-20 mL/minute: Administer 45% of normal dose
- Cl_{cr} 5-10 mL/minute: Administer 40% of normal dose

-The Canadian labeling recommends the following adjustment: Cl_{cr} ≤40 mL/minute: Reduce dose by 40% to 75%.
-The following adjustments have also been recommended:
Aronoff, 2007: Adults: Continuous renal replacement therapy (CRRT): Administer 75% of dose
Kintzel, 1995: Adults:

- Cl_{cr} 46-60 mL/minute: Administer 70% of dose
- Cl_{cr} 31-45 mL/minute: Administer 60% of dose
- Cl_{cr} <30 mL/minute: Consider use of alternative drug

Hepatic Impairment:

No dosage adjustment provided in the manufacturer's labeling (has not been studied); however, adjustment for hepatic impairment is not necessary (King, 2001).

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Fixed doses (dosing which is independent of body weight or BSA), are used in some protocols (eg, testicular cancer); due to toxicity concerns, the same fixed dose should also be considered for obese patients (Griggs, 2012).

Dosing: Adjustment for Toxicity

Pulmonary changes: Discontinue until determined not to be drug-related.

Pulmonary diffusion capacity for carbon monoxide (DL_{CO}) <30% to 35% of baseline: Discontinue treatment.

Common side effect:

>10%:

Dermatologic: Pain at the tumor site, phlebitis. About 50% of patients develop erythema, rash, striae, induration, hyperkeratosis, vesiculation, and peeling of the skin, particularly on the palmar and plantar surfaces of the hands and feet. Hyperpigmentation (50%), alopecia, nailbed changes may also occur. These effects appear dose related and reversible with discontinuation.

Gastrointestinal: Stomatitis and mucositis (30%), anorexia, weight loss

Respiratory: Tachypnea, rales, acute or chronic interstitial pneumonitis, and pulmonary fibrosis (5% to 10%); hypoxia and death (1%). Symptoms include cough, dyspnea, and bilateral pulmonary infiltrates. The pathogenesis is not certain, but may be due to damage of pulmonary, vascular, or connective tissue. Response to steroid therapy is variable and somewhat controversial.

Miscellaneous: Acute febrile reactions (25% to 50%)

1% to 10%:

Dermatologic: Skin thickening, diffuse scleroderma, onycholysis, pruritus

Miscellaneous: Anaphylactoid-like reactions (characterized by hypotension, confusion, fever, chills, and wheezing; onset may be immediate or delayed for several hours); idiosyncratic reactions (1% in lymphoma patients)

Pregnancy Risk Factor: D