Epirubicin

Class: Antineoplastic Agent, Anthracycline

Indications:
_Breast cancer, adjuvant treatment
_Esophageal cancer Gastric cancer

Available dosage form in the hospital:
10 mg vial
EPIRUBICIN HCL 50 mg VIAL
EPIRUBICIN HCL 2 mg/ML VIAL

Trade Names:
Ellence
Pharmorubicin

Doses: Note: Patients receiving 120 mg/m^2/cycle as part of combination therapy (CEF-120 regimen) should also receive prophylactic therapy with sulfamethoxazole/trimethoprim or a fluoroquinolone. Details concerning dosing in combination regimens should also be consulted. Lower starting doses may be necessary for heavily pretreated patients, patients with pre-existing myelosuppression, or with bone marrow involvement.

-Breast cancer, adjuvant treatment:
I.V.: Usual dose: 100-120 mg/m^2 per 3- or 4-week treatment cycle as follows:
- 60 mg/m^2 on days 1 and 8 every 28 days for 6 cycles in combination with cyclophosphamide and fluorouracil (CEF-120 regimen; Levine, 2005)
- **Or** 100 mg/m^2 on day 1 every 21 days for 6 cycles in combination with cyclophosphamide and fluorouracil

-Breast cancer (unlabeled regimens; as a part of combination chemotherapy):
I.V.:
60 mg/m^2 on day 1 every 21 days for 8 cycles (EC regimen; Piccart, 2001)
or 75 mg/m^2 on day 1 every 21 days for 4 cycles (FEC regimen; Buzdar, 2005)
or 75 mg/m^2 on day 1 every 21 days for 6 cycles (EP and EC regimens; Langley, 2005)
or 90 mg/m^2 on day 1 every 21 days for 4 or 6 cycles (FEC regimen ± paclitaxel; Martin, 2008)
or 50 mg/m^2 on days 1 and 8 every 21-28 days for 6-9 cycles

-Esophageal cancer (unlabeled use; as part of combination chemotherapy):I.V.:
50 mg/m^2 on day 1 every 21 days for up to 8 cycles (ECF, ECX, EOF, and EOX regimens; Cunningham, 2008 0
or50 mg/m^2 on day 1 every 21 days for 3 preoperative and 3 postoperative cycles (ECF regimen; Cunningham, 2006)

-Gastric cancer (unlabeled use; as part of combination chemotherapy): I.V.:
50 mg/m^2 on day 1 every 21 days for up to 8 cycles (ECF, ECX, EOF, and EOX regimens [Cunningham, 2008]; ECF regimen [Waters, 1999])
Or 50 mg/m^2 on day 1 every 21 days for 3 preoperative and 3 postoperative cycles (ECF regimen; Cunningham, 2006)

Dosage modifications (breast cancer; labeled dosing):
-Delay day 1 dose until platelets are ≥100,000/mm^3, ANC ≥1500/mm^3, and no hematologic toxicities have recovered to ≤grade 1
-Reduce day 1 dose in subsequent cycles to 75% of previous day 1 dose if patient experiences nadir platelet counts <50,000/mm^3, ANC <250/mm^3, neutropenic fever, or grade 3/4 no hematologic toxicity during the previous cycle

-For CEF-120 regimen, reduce day 8 dose to 75% of day 1 dose if platelet counts are 75,000-100,000/mm^3 and ANC is 1000-1499/mm^3; omit day 8 dose if platelets are <75,000/mm^3, ANC <1000/mm^3, or grade 3/4 no hematologic toxicity.

-Dosage adjustment in bone marrow dysfunction: Heavily-treated patients, patients with pre-existing bone marrow depression or neoplastic bone marrow infiltration: Lower starting doses (75-90 mg/m^2) should be consider**.**

Geriatric

Plasma clearance of epirubicin in elderly female patients was noted to be reduced by 35%. Although no initial dosage reduction is specifically recommended, particular care should be exercised in monitoring toxicity and adjusting subsequent dosage in elderly patients (particularly females >70 years of age).

Renal Impairment:

The manufacturer's labeling recommends lower doses (dose not specified) in patients with severe renal impairment (serum creatinine >5 mg/dL). Other sources (Aronoff, 2007) suggest no dosage adjustment is needed for Cl_{cr} <50 mL/minute.

Hepatic Impairment:

The manufacturer's labeling recommends the following adjustments (based on clinical trial information):

- Bilirubin 1.2-3 mg/dL or AST 2-4 times the upper limit of normal: Administer 50% of recommended starting dose
- Bilirubin >3 mg/dL or AST >4 times the upper limit of normal: Administer 25% of recommended starting dose

Severe hepatic impairment: Use is not recommended (has not been studied).

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Common side effect:

Central nervous system: Lethargy (1% to 46%)
Dermatologic: Alopecia (70% to 96%)
Endocrine & metabolic: Amenorrhea (69% to 72%), hot flashes (5% to 39%)
Gastrointestinal: Nausea/vomiting (83% to 92%; grades 3/4: 22% to 25%), mucositis (9% to 59%; grades 3/4: ≤9%), diarrhea (7% to 25%)
Hematologic: Leukopenia (50% to 80%; grades 3/4: 2% to 59%), neutropenia (54% to 80%; grades 3/4: 11% to 67%; nadir: 10-14 days; recovery: by day 21), anemia (13% to 72%; grades 3/4: ≤6%), thrombocytopenia (5% to 49%; grades 3/4: ≤5%)
Local: Injection site reactions (3% to 20%; grades 3/4: <1%)
Ocular: Conjunctivitis (1% to 15%)
Miscellaneous: Infection (15% to 22%; grades 3/4: ≤2%)

Pregnancy Risk Factor: D