

Epirubicin: Drug information

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(For additional information [see "Epirubicin: Patient drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

ALERT: US Boxed Warning

Experienced physician:

Epirubicin should be administered only under the supervision of a health care provider who is experienced in the use of cancer chemotherapeutic agents.

Extravasation:

Severe local tissue necrosis will occur if there is extravasation during administration. Epirubicin must not be given by the intramuscular or subcutaneous route.

Myocardial toxicity:

Cardiac toxicity, including fatal congestive heart failure (CHF), may occur either during therapy with epirubicin or months to years after termination of therapy. The probability of developing clinically evident CHF is estimated as approximately 0.9% at a cumulative dose of 550 mg/m², 1.6% at 700 mg/m², and 3.3% at 900 mg/m². In the adjuvant treatment of breast cancer, the maximum cumulative dose used in clinical trials was 720 mg/m². The risk of developing CHF increases rapidly with increasing total cumulative doses of epirubicin in excess of 900 mg/m²; this cumulative dose should only be exceeded with extreme caution. Active or dormant cardiovascular disease, prior or concomitant radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, or concomitant use of other cardiotoxic drugs may increase the risk of cardiac toxicity. Cardiac toxicity with epirubicin may occur at lower cumulative doses whether or not cardiac risk factors are present.

Secondary malignancy:

Secondary acute myeloid leukemia (AML) has been reported in patients with breast cancer treated with anthracyclines, including epirubicin. The occurrence of refractory secondary leukemia is more common when such drugs are given in combination with DNA-damaging antineoplastic agents, when patients have been heavily pretreated with cytotoxic drugs, or when doses of anthracyclines have been escalated. The cumulative risk of developing treatment-related AML or myelodysplastic syndrome (MDS), in 7,110 patients with breast cancer who received adjuvant treatment with epirubicin-containing regimens, was estimated as 0.27% at 3 years, 0.46% at 5 years, and 0.55% at 8 years.

Hepatic impairment:

Dosage should be reduced in patients with impaired hepatic function.

Bone marrow suppression:

Severe myelosuppression may occur.

Brand Names: US Ellence

Brand Names: Canada Ellence; Epirubicin for Injection; Epirubicin Hydrochloride Injection; Pharmorubicin

Pharmacologic Category Antineoplastic Agent, Anthracycline; Antineoplastic Agent, Topoisomerase II Inhibitor

Dosing: Adult **Note:** Patients receiving 120 mg/m²/cycle as part of combination therapy (CEF-120 regimen) should also receive prophylactic antibiotic therapy with sulfamethoxazole/trimethoprim or a fluoroquinolone. Lower starting doses may be necessary for heavily pretreated patients, patients with preexisting myelosuppression, or with bone marrow involvement. If clinically reasonable, delay epirubicin therapy until other cardiotoxic agents with long half-lives (eg, trastuzumab) have been cleared. The recommended lifetime maximum dose is 900 mg/m². Epirubicin is associated with a moderate to high emetic potential (depending on dose or regimen); antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Dupuis 2011; Roila 2016).

Breast cancer, adjuvant treatment: IV: Usual dose: 100 to 120 mg/m² per 3- or 4-week treatment cycle as follows:

60 mg/m² 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/m² on day 1 every 21 days for 6 cycles in combination with cyclophosphamide and fluorouracil (FEC-100 regimen; Bonneterre 2005) **or**

Breast cancer (off-label regimens): IV:

EC regimen: 100 mg/m² on day 1 every 21 days for 8 cycles in combination with cyclophosphamide (Piccart 2001) **or**

EP or EC regimen: 75 mg/m² on day 1 every 21 days for up to 6 cycles in combination with either paclitaxel or cyclophosphamide (Langley 2005) **or**

FEC regimen ± paclitaxel: 90 mg/m² on day 1 every 21 days for 6 cycles in combination with fluorouracil and cyclophosphamide or for 4 cycles in combination with fluorouracil and cyclophosphamide followed by paclitaxel (Martin 2008) **or**

FEC regimen followed by pertuzumab + trastuzumab + docetaxel: 100 mg/m² on day 1 every 21 days for 3 cycles in combination with fluorouracil and cyclophosphamide, followed by 3 cycles of pertuzumab, trastuzumab, and docetaxel (Schneeweiss 2013) **or**

CEF regimen: 50 mg/m² on days 1 and 8 every 21 or 28 days for 6 to 9 cycles in combination with cyclophosphamide and fluorouracil (Ackland 2001)

Esophageal cancer (off-label use): IV:

ECF, ECX, EOF, and EOX regimens: 50 mg/m² on day 1 every 21 days for up to 8 cycles in combination with cisplatin (C), oxaliplatin (O), fluorouracil (F), and/or capecitabine (X) (Cunningham 2008) **or**

ECF regimen: 50 mg/m² on day 1 every 21 days for 3 preoperative and 3 postoperative cycles in combination with cisplatin and fluorouracil (Cunningham 2006)

Gastric cancer (off-label use): IV:

ECF, ECX, EOF, and EOX regimens: 50 mg/m² on day 1 every 21 days for up to 8 cycles in combination with cisplatin (C), oxaliplatin (O), fluorouracil (F), and/or capecitabine (X) (Cunningham 2008; Waters 1999) **or**

ECF regimen: 50 mg/m² on day 1 every 21 days for 3 preoperative and 3 postoperative cycles in combination with cisplatin and fluorouracil (Cunningham 2006)

Osteosarcoma (off-label use): IV: 90 mg/m² on day 1 every 21 days for 3 cycles before surgery and 90 mg/m² on day 1 every 28 days for 3 cycles after surgery (in combination with cisplatin, ifosfamide and mesna) (Basaran 2007)

Soft tissue sarcoma (off-label use): IV: 25 mg/m² on days 1, 2, and 3 every 28 days for 4 cycles (in combination with ifosfamide and mesna) (Petrioli 2002) **or** 60 mg/m² on days 1 and 2 every 21 days for 5 cycles (in combination with ifosfamide, mesna, and filgrastim) (Frustaci 2001)

Dosage adjustment for toxicity (breast cancer; labeled dosing):

Note: Heavily-treated patients, patients with preexisting bone marrow depression or neoplastic bone marrow infiltration: Lower starting doses (75 to 90 mg/m²) should be considered.

Delay day 1 dose of subsequent cycles until platelets are $\geq 100,000/\text{mm}^3$, ANC $\geq 1500/\text{mm}^3$, and nonhematologic toxicities have recovered to \leq grade 1

Reduce day 1 dose in subsequent cycles to 75% of previous day 1 dose if patient experiences nadir platelet counts $< 50,000/\text{mm}^3$, ANC $< 250/\text{mm}^3$, neutropenic fever, or grade 3/4 nonhematologic 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 to 100,000/mm³ and ANC is 1000 to 1499/mm³; omit day 8 dose if platelets are $< 75,000/\text{mm}^3$, ANC $< 1000/\text{mm}^3$, or grade 3/4 nonhematologic toxicity

Dosing: 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).

Dosing: 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 CrCl < 50 mL/minute.

Dosing: Hepatic Impairment The manufacturer's labeling recommends the following adjustments

(based on clinical trial information):

Bilirubin 1.2 to 3 mg/dL or AST 2 to 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).

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Solution, Intravenous, as hydrochloride [preservative free]:

Ellence: 50 mg/25 mL (25 mL); 200 mg/100 mL (100 mL)

Generic: 50 mg/25 mL (25 mL); 200 mg/100 mL (100 mL)

Solution Reconstituted, Intravenous, as hydrochloride:

Generic: 50 mg (1 ea [DSC])

Generic Equivalent Available (US) Yes

Administration Epirubicin is associated with a moderate to high emetic potential (depending on dose or regimen); antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Dupuis 2011; Roila 2016).

IV: Infuse over 15 to 20 minutes or slow IV push; if lower doses due to dose reduction are administered, may reduce infusion time proportionally. Do not infuse over <3 minutes. Infuse into a free-flowing IV solution (NS or D₅W). Avoid the use of veins over joints or in extremities with compromised venous or lymphatic drainage.

Vesicant; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevate extremity. Initiate antidote (dexrazoxane or dimethyl sulfate [DMSO]). Apply dry cold compresses for 20 minutes 4 times daily for 1 to 2 days (Perez Fidalgo 2012); withhold cooling beginning 15 minutes before dexrazoxane infusion; continue withholding cooling until 15 minutes after infusion is completed. Topical DMSO should not be administered in combination with dexrazoxane; may lessen dexrazoxane efficacy.

Dexrazoxane: Adults: 1,000 mg/m² (maximum dose: 2,000 mg) IV (administer in a large vein remote from site of extravasation) over 1 to 2 hours days 1 and 2, then 500 mg/m² (maximum dose: 1,000 mg) IV over 1 to 2 hours day 3; begin within 6 hours of extravasation. Day 2 and day 3 doses should be administered at approximately the same time (\pm 3 hours) as the dose on day 1 (Mouridsen 2007; Perez Fidalgo 2012). **Note:** Reduce dexrazoxane dose by 50% in patients with moderate to severe renal impairment (CrCl <40 mL/minute).

DMSO: Children and Adults: Apply topically to a region covering twice the affected area every 8 hours for 7 days; begin within 10 minutes of extravasation; do not cover with a dressing (Perez Fidalgo 2012).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use Breast cancer, adjuvant treatment: Adjuvant therapy component for primary breast cancer in patients with evidence of axillary node involvement following tumor resection

Use: Off-Label

Esophageal cancer; Gastric cancer; Osteosarcoma; Soft tissue sarcoma

Medication Safety Issues

Sound-alike/look-alike issues:

EpiRUBicin may be confused with DOXOrubicin, DAUNOrubicin, eriBULin, IDArubicin

International issues:

Ellence [US] may be confused with Elase brand name for dornase alfa [Chile, France, Malaysia]

High alert medication:

This drug is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions Frequency not always defined. Percentages reported as part of combination chemotherapy regimens.

Cardiovascular: Decreased left ventricular ejection fraction (asymptomatic; delayed: 1% to 2%), cardiac failure ($\leq 2\%$), atrioventricular block, bradycardia, bundle branch block, cardiac arrhythmia, cardiomyopathy, ECG abnormality, myocarditis, non-specific T wave on ECG, sinus tachycardia, ST segment changes on ECG, tachyarrhythmia, thromboembolism, ventricular premature contractions, ventricular tachycardia

Central nervous system: Lethargy (1% to 46%)

Dermatologic: Alopecia (70% to 96%), skin rash (1% to 9%), skin changes (1% to 5%)

Endocrine & metabolic: Amenorrhea (69% to 72%), hot flash (5% to 39%)

Gastrointestinal: Nausea and vomiting (83% to 92%; grades 3/4: 22% to 25%), mucositis (9% to 59%; grades 3/4: $\leq 9\%$), diarrhea (7% to 25%), anorexia (2% to 3%), abdominal pain, esophagitis, neutropenic enterocolitis, stomatitis, toxic megacolon

Genitourinary: Menopause (premature or early)

Hematologic & oncologic: Neutropenia (54% to 80%; grades 3/4: 11% to 67%; nadir: 10 to 14 days; recovery: by day 21), leukopenia (50% to 80%; grades 3/4: 2% to 59%), anemia (13% to 72%; grades 3/4: $\leq 6\%$), thrombocytopenia (5% to 49%; grades 3/4: $\leq 5\%$), febrile neutropenia (grades 3/4: $\leq 6\%$), acute lymphocytic leukemia, acute myelocytic leukemia, myelodysplastic syndrome

Hepatic: Ascites, hepatomegaly, increased serum transaminases

Hypersensitivity: Hypersensitivity reaction

Infection: Infection (15% to 22%; grades 3/4: $\leq 2\%$)

Local: Injection site reaction (3% to 20%; grades 3/4: $< 1\%$)

Ophthalmic: Conjunctivitis (1% to 15%)

Respiratory: Dyspnea, pulmonary edema

Miscellaneous: Fever (1% to 5%)

$< 1\%$, postmarketing, case reports: Anaphylaxis, arterial embolism, burning sensation of gastrointestinal tract, chills, dehydration, erythema, flushing, gastrointestinal erosion, gastrointestinal hemorrhage, gastrointestinal pain, gastrointestinal ulcer, hyperuricemia, nail hyperpigmentation, oral mucosa hyperpigmentation, phlebitis, pneumonia, pulmonary embolism, radiation recall phenomenon, red urine discoloration, sepsis, shock, skin hyperpigmentation, skin photosensitivity, thrombophlebitis, urticaria

Contraindications

Hypersensitivity to epirubicin, other anthracyclines, anthracenediones, or any component of the formulation; cardiomyopathy and/or heart failure, recent myocardial infarction, severe arrhythmias; previous treatment with anthracyclines up to the maximum cumulative dose

Canadian labeling: Additional contraindications (not in the US labeling): Marked persistent myelosuppression induced by prior treatment with other chemotherapy agents or by radiotherapy; severe hepatic impairment.

Warnings/Precautions

Concerns related to adverse effects:

- Bone marrow suppression: **[US Boxed Warning]: May cause severe myelosuppression**, including leukopenia, thrombocytopenia, and anemia. Myelosuppression is the dose-limiting toxicity. Obtain baseline and periodic blood counts. Patients should recover from myelosuppression due to prior chemotherapy treatment before beginning treatments. Severe neutropenia and severe infections may require supportive care.
- Extravasation: **[US Boxed Warning]: For IV administration only. Vesicant; if extravasation occurs, severe local tissue damage and necrosis may occur. Not for IM or SubQ use.** Injection into a small vein or repeated administration in the same vein may result in venous sclerosis. Ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation. If perivenous infiltration occurs, immediately discontinue infusion and restart in another vein.
- Gastrointestinal toxicity: Epirubicin is associated with a moderate to high emetic potential (depending on dose or regimen); antiemetics are recommended to prevent nausea and vomiting (Basch 2011; Dupuis 2011; Roila 2016).
- Myocardial toxicity: **Myocardial toxicity, including fatal heart failure (HF) may occur, particularly in patients who have received prior anthracyclines (or anthracenediones), prior or concomitant radiotherapy to the mediastinal/pericardial area, who have preexisting cardiac disease (active or dormant), or with concomitant cardiotoxic medications. Cardiotoxicity may be concurrent or delayed (months to years after treatment). The risk of HF is ~0.9% at a cumulative dose of 550 mg/m², ~1.6% at a cumulative dose of 700 mg/m², and ~3.3% at a cumulative dose of 900 mg/m². Cardiotoxicity may also occur at lower cumulative doses or without risk factors. The risk of delayed cardiotoxicity increases more steeply with cumulative doses >900 mg/m², and this dose should be exceeded only with extreme caution. The maximum cumulative dose used in adjuvant studies was 720 mg/m².** Cardiotoxicity is dose-limiting. Early toxicity may consist of tachyarrhythmias, including sinus tachycardia, premature ventricular contractions, and ventricular tachycardia, as well as bradycardia. Electrocardiographic changes including ST-T wave changes, atrioventricular and bundle-branch block have also been reported. These effects are not necessarily predictive of subsequent delayed cardiotoxicity. Delayed toxicity is typically caused by cardiomyopathy which presents as decreased left ventricular ejection fraction (LVEF) and/or signs/symptoms of HF (eg, tachycardia, dyspnea, pulmonary edema, edema, hepatomegaly, ascites, pleural effusion, gallop rhythm). Total cumulative dose should take into account prior treatment with other anthracyclines or anthracenediones, previous or concomitant treatment with other cardiotoxic agents or irradiation of chest. Although the risk increases with cumulative dose, irreversible cardiotoxicity may occur at any dose level. Patients with active or dormant cardiovascular disease, concurrent administration of cardiotoxic drugs, prior therapy with other anthracyclines or anthracenediones, prior or concurrent chest irradiation, advanced age, and infants and children are at increased risk. Children are at increased risk for developing delayed cardiotoxicity. Regular monitoring of LVEF and discontinuation at the first sign of impairment is recommended especially in patients with cardiac risk factors or impaired cardiac function. Discontinue treatment with signs of decreased LVEF. The half-life of other cardiotoxic agents (eg, trastuzumab) must be considered in sequential therapy.
- Secondary malignancy: **[US Boxed Warning]: Treatment with anthracyclines (including epirubicin) may increase the risk of secondary acute myeloid leukemia (AML). AML is more**

common when given in combination with other antineoplastic agents, in patients who have received multiple courses of previous chemotherapy, or with escalated anthracycline doses. In breast cancer patients, the risk for treatment-related AML or myelodysplastic syndrome (MDS) was estimated at 0.27% at 3 years, 0.46% at 5 years, and 0.55% at 8 years after treatment. The latency period for secondary leukemias may be short (1 to 3 years).

- Thromboembolic events: Thrombophlebitis and thromboembolic phenomena (including pulmonary embolism) have occurred.
- Tumor lysis syndrome: May cause tumor lysis syndrome (TLS). Although TLS does not generally occur in patients with breast cancer, if TLS risk is suspected, consider monitoring serum uric acid, potassium, calcium, phosphate and serum creatinine after initial administration; hydration and antihyperuricemic prophylaxis may minimize potential TLS complications.

Disease-related concerns:

- Hepatic impairment: **[US Boxed Warning]: Dosage reduction is recommended in patients with mild-to-moderate hepatic impairment;** use is not recommended in severe hepatic impairment. Evaluate hepatic function at baseline and during treatment. Epirubicin is predominantly hepatically eliminated; impaired hepatic function may lead to increased exposure and toxicity.
- Renal impairment: Dosage reduction is recommended in patients with serum creatinine >5 mg/dL. Evaluate renal function at baseline and during treatment. Has not been studied in patients on dialysis.

Concurrent drug therapy issues:

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

- Elderly: Women ≥70 years of age should be closely monitored for toxicity.
- Pediatric: Children may be at increased risk for developing acute and delayed cardiotoxicity; long-term periodic cardiac function monitoring is recommended.
- Radiation recipients: Epirubicin may have radiosensitizing activity; radiation recall (inflammatory) has also been reported.

Other warnings/precautions:

- Appropriate use: Patients should recover from acute toxicities (stomatitis, myelosuppression, infections) prior to initiating treatment. Assess baseline labs (blood counts, bilirubin, ALT, AST, serum creatinine) and cardiac function (with LVEF). Prophylactic antibiotics should be administered with the CDF-120 regimen.
- Experienced physician: **[US Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician.**
- Immunizations: Patients should not be immunized with live viral vaccines during or shortly after treatment. Inactivated vaccines may be administered (response may be diminished).

Metabolism/Transport Effects None known.

Drug Interactions

(For additional information: [Launch drug interactions program](#)) Lexicomp®

Ado-Trastuzumab Emtansine: May enhance the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). Management: When possible, patients treated with ado-trastuzumab emtansine should avoid anthracycline-based therapy for up to 7 months after stopping ado-trastuzumab emtansine. Monitor closely for cardiac dysfunction in patients receiving this combination. *Risk D: Consider therapy modification*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bevacizumab: May enhance the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). *Risk C: Monitor therapy*

Cardiac Glycosides: May diminish the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). Antineoplastic Agents (Anthracycline, Systemic) may decrease the serum concentration of Cardiac Glycosides. The effects of liposomal formulations may be unique from those of the free drug, as liposomal formulation have unique drug disposition and toxicity profiles, and liposomes themselves may alter digoxin absorption/distribution. *Risk C: Monitor therapy*

Cimetidine: May increase the serum concentration of EpiRUBicin. *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Cyclophosphamide: May enhance the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D:*

Consider therapy modification

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Taxane Derivatives: May enhance the adverse/toxic effect of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may increase the serum concentration of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may also increase the formation of toxic anthracycline metabolites in heart tissue. *Risk D: Consider therapy modification*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). Management: When possible, patients treated with trastuzumab should avoid anthracycline-based

therapy for up to 7 months after stopping trastuzumab. Monitor closely for cardiac dysfunction in patients receiving anthracyclines with trastuzumab. *Risk D: Consider therapy modification*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Pregnancy Risk Factor D ([show table](#))

Pregnancy Implications Adverse events were observed in animal reproduction studies. Women of childbearing potential should be advised to use effective contraception and avoid becoming pregnant during treatment. Men undergoing treatment should use effective contraception. Epirubicin may cause irreversible amenorrhea in premenopausal women.

Limited information is available from a retrospective study of women who received epirubicin (in combination with cyclophosphamide or weekly as a single-agent) during the second or third (prior to week 35) trimester for the treatment of pregnancy-associated breast cancer (Ring 2005) and from a study of women who received epirubicin (weekly as a single-agent) at gestational weeks 16 through 30 for the treatment of pregnancy-associated breast cancer (Peccatori 2009). Some pharmacokinetic properties of epirubicin may be altered in pregnant women (van Hasselt 2014). The European Society for Medical Oncology (ESMO) has published guidelines for diagnosis, treatment, and follow-up of cancer during pregnancy (Peccatori 2013); the guidelines recommend referral to a facility with expertise in cancer during pregnancy and encourage a multidisciplinary team (obstetrician, neonatologist, oncology team). If chemotherapy is indicated, it should not be administered in the first trimester, but may begin in the second trimester. There should be a 3-week time period between the last chemotherapy dose and anticipated delivery, and chemotherapy should not be administered beyond week 33 of gestation.

A pregnancy registry is available for all cancers diagnosed during pregnancy at Cooper Health (877-635-4499).

Breast-Feeding Considerations It is not known if epirubicin is present in human breast milk; however, other anthracyclines are excreted in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, the manufacturer recommends a decision be made to discontinue breastfeeding or to discontinue the drug, taking into account the importance of treatment to the mother.

Monitoring Parameters Baseline and repeated measurements of CBC with differential, liver function tests, serum creatinine, electrolytes, ECG, and LVEF. The method used for assessment of LVEF (echocardiogram or MUGA) should be consistent during routine monitoring. Monitor injection site during infusion for possible extravasation or local reactions.

Mechanism of Action Epirubicin is an anthracycline antineoplastic agent; known to inhibit DNA and

RNA synthesis by steric obstruction after intercalating between DNA base pairs; active throughout entire cell cycle. Intercalation triggers DNA cleavage by topoisomerase II, resulting in cytotoxic activity. Also inhibits DNA helicase, and generates cytotoxic free radicals.

Pharmacodynamics/Kinetics

Distribution: V_{dss} : 21 to 27 L/kg

Protein binding: ~77% to albumin

Metabolism: Extensively via hepatic and extrahepatic (including RBCs) routes

Half-life elimination: Triphasic; Mean terminal: 33 hours

Excretion: Feces (34% to 35%); urine (20% to 27%)

Pricing: US

Solution (Ellence Intravenous)

50 mg/25 mL (25 mL): \$67.20

200 mg/100 mL (100 mL): \$268.80

Solution (EpiRUBicin HCl Intravenous)

50 mg/25 mL (25 mL): \$72.00

200 mg/100 mL (100 mL): \$279.98

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names 4-Epeedo-50 (ET); Adricin (LK); Ai Da Sheng (CN); Anthracin (JO); Binarin (MX); Bioepicycyna (PL); Ciazil (ID, JO, VN); E.P.Mycin (PH); Eberubi (SG); Ecclepia (RO); Epicin (BD, MY, TW); Epidoxo (PY); Epifil (AR); Epilem (MX, TH); Epilim (CR, DO, GT, HN, NI, PA, SV); Epirol (ID); Epiruba (LK); Episindan (HK, HR, SG); Epivid (PH); Ericina (CO); Eutsyn (UA); Farmorrubicina RTU (CL); Farmorubicin (AE, AT, BH, CH, CY, CZ, DE, DK, EG, FI, GR, HR, HU, IL, IN, IQ, IR, JO, JP, KW, LB, LU, LY, MX, OM, PK, PL, QA, RU, SA, SE, SI, SK, SY, TR, VE, YE, ZA); Farmorubicin CSU (ZA); Farmorubicin PFS (BG, EE, LV); Farmorubicin RD (BG, EE, LV, MX, ZA); Farmorubicina (ES, IT, PE, PT, VN); Farmorubicina CS (BR, CO, EC); Farmorubicina R.D. (BR); Farmorubicine (BE, FR, NL); Favicin (CR, DO, GT, HN, NI, PA, SV); Grubin (BD); Neoquabin (PH); Panbicin (TW); Pharmarubicin RD (CN); Pharmorubicin (AU, GB, HK, IE, MY, NZ, PH); Pharmorubicin CS (SG, TH); Pharmorubicin PDF (KR); Pharmorubicin PFS (KR, TW); Rubimeda (UA); Rubisandin (ID, LK); Vizpirub (UA)

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