DRUG NAME: Epirubicin

SYNONYM(S): 4'-epidoxorubicin, [1] IMI-28, [1] NSC-256942 [1]

COMMON TRADE NAME(S): PHARMORUBICIN®, [2] ELLENCE® [3]

CLASSIFICATION: anthracycline antineoplastic antibiotic [4]

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

The mechanism of action of epirubicin appears to be related to its ability to bind to nucleic acids. [2] It forms a complex with DNA by intercalation between base pairs, resulting in inhibition of DNA and RNA synthesis. [4] Intercalation also triggers DNA cleavage by topoisomerase II, resulting in cytocidal activity. [3,4] Binding to cell membranes and plasma proteins may also be involved. [2] Epirubicin also generates cytotoxic free radicals. [3,4] Epirubicin is the 4'-epimer of doxorubicin; i.e., there is a different spatial orientation of the hydroxyl group at the 4' carbon of the sugar moiety. [4] This difference may account for faster elimination and reduced toxicity. [2]

PHARMACOKINETICS:

Distribution	rapidly and widely distributed into tissues; may concentrate in red blood cells, whole blood concentrations are approximately twice those of plasma	
	cross blood brain barrier?	no
	volume of distribution	21-27 L/kg
	plasma protein binding	77%
Metabolism	extensive hepatic metabolism; also metabolized by other organs and cells, including red blood cells	
	active metabolite(s)	epirubicinol (13-OH epirubicin) ; cytotoxic activity one-tenth that of epirubicin; plasma levels consistently lower than epirubicin
	inactive metabolite(s)	glucuronides of epirubicin and epirubicinol; doxorubicin; aglycones of doxorubicinol, 7-deoxydoxorubicin, and 7-deoxydoxorubicinol
Excretion	predominantly hepatobiliary; rapid elimination of parent compound from plasma	
	urine	9-10% within 48 h [2]; 20-27% within 4 days
	feces	40% of dose recovered in bile within 72 h
	terminal half life	33 h
	clearance	65-83 L/h
Gender	no differences observed	
Elderly	clearance may be decreased in elderly women	

Adapted from standard reference [3] unless specified otherwise.

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USES:

Primary uses:
* Breast cancer
* Gastric cancer
* Lung cancer, non-small cell
* Lung cancer, small cell
* Lymphoma, Hodgkin's
* Lymphoma, non-Hodgkin's
* Ovarian cancer

*Health Canada approved indication

Other uses:
Bladder cancer [5,6]
Pediatric, soft tissue sarcoma [7]
Soft tissue sarcoma [8-10]

SPECIAL PRECAUTIONS:

Contraindications:
- history of hypersensitivity reaction to hypersensitivity to epirubicin, other anthracyclines (e.g., daunorubicin, doxorubicin), or anthracenediones (e.g., mitoxantrone, mitomycin) [3]
- severe hepatic impairment [3]
- severe myocardial insufficiency, recent myocardial infarction, severe arrhythmias, or history of severe cardiac disease [3]

Caution:
- ***cardiac toxicity*** may be manifested by early (acute) or late (delayed) effects [4]; assess cardiac function at baseline and continue during treatment.
- ***risk factors*** for developing epirubicin-induced cardiotoxicity include [3]:
  - high cumulative dose, previous therapy with other anthracyclines or anthracenediones
  - prior or concomitant radiotherapy to the mediastinal/pericardial area
  - pre-existing heart disease
  - concomitant use of drugs that can suppress cardiac contraction

Carcinogenicity: Epirubicin has been associated with an increased risk of secondary leukemia in human trials. Epirubicin was also shown to have considerable carcinogenic activity in *in vivo* carcinogenesis studies in animals.[11]

Mutagenicity: Epirubicin is mutagenic and clastogenic in animals, and may induce chromosomal damage in human spermatozoa. [11]

Fertility: There is no conclusive information about epirubicin adversely affecting human fertility. Epirubicin may cause amenorrhea or premature menopause in premenopausal women. [11] Dose-related infertility has been observed in mammals of both sexes. [3]

Pregnancy: There is no conclusive evidence that epirubicin causes teratogenesis in humans. In animal studies, epirubicin in high doses was embryotoxic and teratogenic in rats and embryotoxic and an abortifacient in rabbits. [11] Chemotherapy protocols including epirubicin have been administered during pregnancy to treat breast cancer. [12-16] For more information, refer to BC Cancer's Cancer Management Manual/Breast Cancer ***Special Circumstances: Breast Cancer in Pregnancy*.**

Breastfeeding is not recommended due to the potential secretion into breast milk.

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they

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were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important. [17]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
allergy/immunology	anaphylaxis
	chills, fever, shock, urticaria
blood/bone marrow/ febrile neutropenia	anemia (13-72%)
	leukopenia (50-80%, severe 2-59%), ***neutropenia*** (54-80%, severe 10-67%); nadir 10-14 days after treatment; recovery by day 21
	neutropenic fever (6%)
	thrombocytopenia (5-49%)
cardiovascular (arrhythmia)	acute transient ECG changes, sinus tachycardia; see discussion following table
cardiovascular (general)	***congestive heart failure***, symptomatic [3] (0.9-3.3%, dose-related); risk increases steeply after cumulative dose of 900 mg/m^2; see paragraph following **Side Effects** table
	decreased left ventricular ejection fraction, asymptomatic (1-3%); see paragraph following **Side Effects** table
	thromboembolism (including fatal pulmonary embolism), thrombophlebitis, venous sclerosis
constitutional symptoms	fever (1-5%)
	fatigue/lethargy (1-46%)
	malaise/asthenia
dermatology/skin	*extravasation hazard:* vesicant[18]
	alopecia (70-96%), regrowth occurs 2-3 months after discontinuing epirubicin therapy [3]
	flushing
	injection site reactions (2-20%)
	photosensitivity
	radiation recall reaction
	rash/itch (1-9%)
	skin changes (1-5%)
	skin and nail hyperpigmentation
endocrine	hot flashes(5-39%)
gastrointestinal	*emetogenic potential:* dose-related [19]; high-moderate for >90 mg/m^2, low-moderate for ≤90 mg/m^2
	anorexia (2-3%)
	dehydration
	diarrhea (7-25%)
	dyspepsia
	hyperpigmentation of the oral mucosa
	mucositis (9-58%)

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ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	nausea/vomiting (83-92%)
hemorrhage	bleeding, GI
hepatic	increased transaminases [20]
infection	***infection*** (15-22%)
metabolic/laboratory	hyperuricemia
ocular/visual	conjunctivitis (1-15%), keratitis
renal/genitourinary	red colouration of urine for 1-2 days after administration
secondary malignancy	acute myeloid leukemia, myelodysplastic syndrome (0.3-0.6%)
sexual/reproductive function	amenorrhea (69-72%), premature menopause
syndromes	tumour lysis syndrome

Adapted from standard reference [3] unless specified otherwise.

Hyperuricemia may result from cell lysis by epirubicin and may lead to electrolyte disturbances or acute renal failure. [21] It is most likely with highly proliferative tumours of massive burden, such as leukemias, high-grade lymphomas, and myeloproliferative diseases. The risk may be increased in patients with preexisting renal dysfunction, especially ureteral obstruction. Suggested prophylactic treatment for high-risk patients [22]:

- aggressive hydration: 3 L/m²/24 hr with target urine output >100 ml/h
- if possible, discontinue drugs that cause hyperuricemia (e.g., thiazide diuretics) or acidic urine (e.g., salicylates)
- monitor electrolytes, calcium, phosphate, renal function, LDH, and uric acid q6h x 24-48 hours
- replace electrolytes as required
- allopurinol 600 mg po initially, then 300 mg po q6h x6 doses, then 300 mg po daily x 5-7 days

Urine should be alkalinized only if the uric acid level is elevated, using sodium bicarbonate IV or PO titrated to maintain urine pH>7. Rasburicase (FASTURTEC®) is a novel uricolytic agent that catalyzes the oxidation of uric acid to a water-soluble metabolite, removing the need for alkalinization of the urine. [23] It may be used for treatment or prophylaxis of hyperuricemia; however, its place in therapy has not yet been established. Aluminum hydroxide (AMPHOGEL®) may be added orally if phosphate becomes elevated. If aluminum hydroxide has been added, discontinue sodium bicarbonate. [24]

Cardiotoxicity is thought to be due to free radical damage as myocardial tissue is susceptible to these highly reactive species. [25] Anthracycline cardiotoxicity may present with early or late effects. [26,27] The following information applies to all anthracyclines, anthracenediones and mitoxantrone. [25,27,28]

Early cardiotoxic effects are not dose-related and may present from mild ECG changes to life-threatening arrhythmias. [25,26,28] These events may occur during or immediately after a single dose of anthracycline treatment, [25,28] but do not predict subsequent development of delayed cardiotoxicity and are not considered indications for suspension of therapy. [25,26,28-31]

Late cardiotoxic effects, which are dose-related and clinically the most important type of cardiotoxic effect, present as reduced LVEF or symptomatic CHF, and typically occur weeks to years after completion of treatment. [25,27-30] Abnormalities in LVEF are associated with all the anthracyclines and their derivatives. [27] LVEF changes are related to the total cumulative dose, are irreversible and refractory to medical therapy. [25,32]

Prevention and treatment: Cardiac assessment should occur at baseline and throughout therapy. Monitor for symptomatic congestive heart failure (CHF) or reduced left ventricular ejection fraction (LVEF). Sensitive, non-

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invasive methods to measure LVEF include radionucleotide angiography (RNA), MUGA, or echocardiogram. [27] Late cardiotoxic effects may be prevented by stopping treatment with the associated anthracycline once patients have reached the suggested maximum cumulative dose. [25,32] Management of anthracycline cardiotoxicity includes discontinuation of the drug and initiating standard treatment of CHF. [27]

Cardiotoxicity risk can be reduced but not eliminated with the use of alternative anthracyclines (i.e., epirubicin or liposomal doxorubicin) or by altering the frequency of administration (once a week vs. once every 3 weeks, or continuous infusion). [27] Cardioprotectant therapy with dexrazoxane may be considered for patients with cumulative doxorubicin-equivalent doses greater than 300 mg/m^2. [28,33,34]

Cumulative doses should be calculated and account for all previous anthracyclines or anthracenediones received during the patient's lifetime. For further information on suggested conversion factors and monitoring thresholds for anthracyclines, see ***Dose Conversion for Anthracyclines Exposure*** in Appendix.

Extravasation of epirubicin can occur with or without accompanying stinging or burning sensation, and even if blood returns well on aspiration of the infusion needle. [3] Severe local tissue necrosis may occur. To minimize the risk of thrombosis or perivenous extravasation, the usual administration time should be 15 to 20 minutes, and never less than 3 minutes. [3] For more information on prevention and treatment of extravasation with epirubicin, refer to BC Cancer Systemic Therapy Policy III-20 ***Prevention and Management of Extravasation of Chemotherapy*****.** Also, monitor for local erythematous streaking along vein and/or facial flushing which may indicate a too rapid infusion rate. [35] This has traditionally been called the "epirubicin flare." [36,37]

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
bevacizumab [38]	anthracycline-induced cardiotoxicity may be increased	unknown	monitor cardiac function throughout treatment
calcium channel blockers (e.g., verapamil) [2,4]	anthracycline-induced cardiotoxicity may be increased	additive toxicity	monitor cardiac function throughout treatment
cimetidine [2,3,39]	increases AUC of epirubicin by 50% and decreases clearance of epirubicin by 30%	unknown; does not seem to be related to cytochrome P450	discontinue cimetidine and choose alternate therapy; e.g., ranitidine
gemcitabine [40]	no influence on epirubicin pharmacokinetics		
taxanes [40-46] (e.g., docetaxel, paclitaxel)	toxicity of both agents may be increased when given concurrently, regardless of which drug is given first; lower neutrophil and platelet nadirs, and slower neutrophil recovery have been observed	increased levels of epirubicin metabolites, decreased taxane clearance	separate administration by 24 hours if possible
trastuzumab [47]	anthracycline-induced cardiotoxicity may be increased	unknown	monitor cardiac function throughout treatment

SUPPLY AND STORAGE:

Injection*:* Teva Canada Limited supplies epirubicin as 10 mg, 20 mg, 50 mg, 150 mg, and 200 mg ready-to-use, single-use (preservative free) vials in a concentration of 2 mg/mL. Refrigerate. Protect6 from light.

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

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SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see Chemotherapy Preparation and Stability Chart in Appendix.

Additional information:

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold***, ***italics***

Subcutaneous [2]	must not be used due to corrosive nature
Intramuscular [2]	must not be used due to corrosive nature
Direct intravenous	into tubing of running IV; see ***Systemic Therapy Policy III-20: Prevention and Management of Extravasation of Chemotherapy***
Intermittent infusion [48-53]	has been used
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical [6,54-58]	has been instilled in the bladder as a single dose postoperatively OR as induction doses of 50-100 mg in 25-100 mL NS weekly for 6 to 8 weeks, followed by monthly maintenance doses to 1 year; solutions are retained for 1-2 h after instillation

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BC Cancer usual dose noted in ***bold, italics***

	Cycle Length:	
Intravenous:	2 weeks [2]:	35 mg/m^2 IV for one dose on day 1 (total dose per cycle 35 mg/m^2)
	3 weeks [59]:	***100 mg/m^2 IV for one dose on day 1*** (total dose per cycle 100 mg/m^2)
	3-4 weeks [2]:	50-150 mg/m^2 IV for one dose on day 1 (total dose per cycle 50-150 mg/m^2)
	4 weeks [60-62]:	***60 mg/m^2 IV for one dose on days 1 and 8***

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BC Cancer usual dose noted in ***bold, italics***

(total dose per cycle 120 mg/m^2)

4 weeks [63-65]: when given as a dose-dense regimen with filgrastim (G-CSF) support:
60 mg/m^2 IV for one dose on days 1 and 15
(total dose per cycle 120 mg/m^2)

Suggested maximum cumulative doses [11,66-68]*:* 1000 mg/m^2

Concurrent radiation: generally not administered concurrently due to additive toxicity [4]

Dosage in myelosuppression: modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix "Dosage Modification for Myelosuppression"

Dosage in renal failure [2]*:* lower starting doses are necessary if serum creatinine >442 micromol/L

Dosage in hepatic failure [2]*:*

AST		Bilirubin	Dose
2-4 X ULN	or	21-51 micromol/L	50%
> 4 x ULN	or	> 51 micromol/L	25%

contraindicated in severe hepatic impairment

Dosage in dialysis: no information found

Children: safety and effectiveness in children has not been studied [3]

REFERENCES:

1. Dorr RT, Von-Hoff DD. Drug monographs. Cancer Chemotherapy Handbook. 2nd ed. Norwalk, Conneticut: Appleton and Lange; 1994. p. 434–439
2. Pfizer Canada Inc. PHARMORUBICIN® product monograph. Kirkland, Quebec; 5 May, 2005.
3. Pfizer Inc. ELLENCE® product monograph. New York, NY; May, 2005.
4. McEvoy GK, editor. AHFS 2005 Drug Information. Bethesda, MD: American Society of Health-System Pharmacists, Inc.; 2005.
5. de Reijke TM, Kurth KH, Sylvester RJ, et al. Bacillus Calmette-Guerin versus epirubicin for primary, secondary or concurrent carcinoma in situ of the bladder: results of a European Organization for the Research and Treatment of Cancer--Genito-Urinary Group Phase III Trial (30906). Journal of Urology ; Feb, 2005;173(2):405–9
6. Rajala P, Kaasinen E, Raitanen M, et al. Perioperative single dose instillation of epirubicin or interferon-alpha after transurethral resection for the prophylaxis of primary superficial bladder cancer recurrence: a prospective randomized multicenter study--FinnBladder III long-term results. J Urol ; Sep, 2002;168(3):981–5
7. Orbach D, Rey A, Oberlin O, et al. Soft tissue sarcoma or malignant mesenchymal tumors in the first year of life: experience of the International Society of Pediatric Oncology (SIOP) Malignant Mesenchymal Tumor Committee. Journal of Clinical Oncology ; Jul 1, 2005;23(19):4363–71
8. Ottaiano A, De Chiara A, Fazioli F, et al. Neoadjuvant chemotherapy for intermediate/high-grade soft tissue sarcomas: five-year results with epirubicin and ifosfamide. Anticancer Research ; Nov-Dec, 2002;22(6B):3555–9
9. Petrioli R, Coratti A, Correale P, et al. Adjuvant epirubicin with or without Ifosfamide for adult soft-tissue sarcoma. American Journal of Clinical Oncology ; Oct, 2002;25(5):468–73
10. Lopez M, Vici P, Di Lauro L, et al. Increasing single epirubicin doses in advanced soft tissue sarcomas. Journal of Clinical Oncology ; Mar 1, 2002;20(5):1329–34
11. Teva Canada Limited. Epirubicin for injection product monograph. Toronto, Ontario; August 20, 2014.
12. Andreadis C, Charalampidou M, Diamantopoulos N, et al. Combined chemotherapy and radiotherapy during conception and first two trimesters of gestation in a woman with metastatic breast cancer. Gynecologic Oncology ; Oct, 2004;95(1):252–255
13. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. The Lancet Oncology ; 2004;5(5):283–291

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Revised: 1 March 2025

14. Gadducci A, Cosio S, Fanucchi A, et al. Chemotherapy with epirubicin and paclitaxel for breast cancer during pregnancy: case report and review of the literature. Anticancer Research ; Nov-Dec, 2003;23(6D):5225–9
15. Goldwasser F, Pico JL, Cerrina J, et al. Successful chemotherapy including epirubicin in a pregnant non-Hodgkin's lymphoma patient. Leukemia & Lymphoma ; Dec, 1995;20(1-2):173–6
16. Muller T, Hofmann J, Steck T. Eclampsia after polychemotherapy for nodal-positive breast cancer during pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology ; August, 1996;67(2):197–198
17. Susan Ellard MD. Medical Oncologist, BC Cancer Agency. Personal Communication. 27 January, 2006.
18. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; March 1 , 2021.
19. BC Cancer Supportive Care Tumour Group. (SCNAUSEA) BC Cancer Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer; September 1 , 2022.
20. Rose BD editor. Epirubicin: Drug Information. : UpToDate®; accessed 30 November, 2005. www.uptodate.com;
21. DeVita VT, Hellman S, Rosenberg SA. Cancer Principles & Practice of Oncology. 6th ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2001. p. 2640
22. Leukemia/Bone Marrow Transplant Program of British Columbia. Leukemia/BMT Manual. 4th ed. Vancouver, British Columbia: Vancouver Hospital and Health Sciences Centre / BC Cancer Agency; 2003. p. 27
23. Sanofi-Synthelabo. FASTURTEC® product information. Markham, Ontario; 2004.
24. Leukemia/Bone Marrow Transplant Program of British Columbia. Leukemia/BMT Manual. E-Edition ed. Vancouver, British Columbia: Vancouver Hospital and Health Sciences Centre / BC Cancer Agency; 2010. p. 93–94
25. Seiter K. Toxicity of the topoisomerase II inhibitors. Expert Opin Drug Saf ; 2005;4(2):219–234
26. Pfizer Canada Inc. IDAMYCIN® product monograph. Kirkland, Quebec; 19 February , 2009.
27. Carver JR, Shapiro CL, Ng A, et al. American Society of Clinical Oncology clinical evidence review on the ongoing care of adult cancer survivors: cardiac and pulmonary late effects. J Clin Oncol ; September 01, 2007;25(25):3991–4008
28. McEvoy GK, editor. AHFS 2005 Drug Information. Bethesda, Maryland: American Society of Health-System Pharmacists, Inc.; 2005.
29. Mayne Pharma (Canada) Inc. Doxorubicin Product Monograph. Montreal, Quebec; 2002.
30. Novopharm Limited. Doxorubicin Product Monograph. Scarborough, Ontario; 1996.
31. Repchinsky C, BSP. Compendium of Pharmaceuticals and Specialties. Ottawa, Ontario: Canadian Pharmacists association; 2005. p. 676
32. Rose BD editor. Cardiotoxicity in patients receiving chemotherapy. Waltham, Massachusetts: UpToDate®; accessed 22 September, 2005.
33. Schuchter LM, Hensley ML, Meropol NJ, et al. 2002 Update of Recommendations for the Use of Chemotherapy and Radiotherapy Protectants: Clinical Practice Guidelines of the American Society of Clinical Oncology. J Clin Oncol ; June 15, 2002;20(12):2895–2903
34. Hensley M, Hagerty K, Kewalramani T, et al. American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants. J Clin Oncol ; 2009;27(1):127–145
35. Rose BD editor. Doxorubicin: Drug Information. : UpToDate®; accessed 31 August, 2005. www.uptodate.com
36. Harwood KV, Aisner J. Treatment of chemotherapy extravasation: current status. Cancer Treatment Reports ; 1984;68(7-8):939–45
37. Boyle DM, Engelking C. Vesicant extravasation: myths and realities. Oncology Nursing Forum ; 1995;22(1):57–67
38. Rose BD editor. Antineoplastic agents (Anthracyclines)/Bevacizumab. www.uptodate.com ed. : UpToDate®; accessed 15 December, 2005. www.uptodate.com
39. Murray LS, Jodrell DI, Morrison JG, et al. The effect of cimetidine on the pharmacokinetics of epirubicin in patients with advanced breast cancer: Preliminary evidence of a potentially common drug interaction. Clinical Oncology (Royal College of Radiologists) ; 1998;10(1):35–38
40. Fogli S, Danesi R, Gennari A, et al. Gemcitabine, epirubicin and paclitaxel: Pharmacokinetic and pharmacodynamic interactions in advanced breast cancer. Annals of Oncology ; 2002;13(6):919–927
41. Baker AF, Dorr RT. Drug interactions with the taxanes: clinical implications. Cancer Treatment Reviews ; Aug, 2001;27(4):221–33
42. Ceruti M, Tagini V, Recalenda V, et al. Docetaxel in combination with epirubicin in metastatic breast cancer: pharmacokinetic interactions. Farmaco ; Nov-Dec, 1999;54(11-12):733–9
43. Danesi R, Conte PF, Del Tacca M. Pharmacokinetic optimisation of treatment schedules for anthracyclines and paclitaxel in patients with cancer. Clinical Pharmacokinetics ; Sep, 1999;37(3):195–211
44. Esposito M, Venturini M, Vannozzi MO, et al. Comparative effects of paclitaxel and docetaxel on the metabolism and pharmacokinetics of epirubicin in breast cancer patients. J Clin Oncol ; 1999;17(4):1132
45. Grasselli G, Vigano L, Capri G, et al. Clinical and pharmacologic study of the epirubicin and paclitaxel combination in women with metastatic breast cancer. Journal of Clinical Oncology ; Apr 15, 2001;19(8):2222–31
46. Venturini M, Lunardi G, Del Mastro L, et al. Sequence effect of epirubicin and paclitaxel treatment on pharmacokinetics and toxicity. Journal of Clinical Oncology ; May, 2000;18(10):2116–25
47. Rose BD editor. Antineoplastic Agents (Anthracycline)/Trastuzumab. : UpToDate®; accessed 15 December, 2005. www.uptodate.com
48. Hospira Healthcare Corporation. Doxorubicin hydrochloride for injection® product monograph. Saint-Laurent, Quebec; 18 February, 2008.

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49. Pharmacia Limited. Pharmorubicin Solution for Injection® product monograph. Sandwich, Kent (United Kingdom); 15 September, 2010.
50. Actavis UK Ltd. Epirubicin hydrochloride 50 mg powder for injection or infusion® product monograph. Barnstaple, Devon (United Kingdom); 12 April, 2011.
51. Hospira UK Ltd. Epirubicin hydrochloride injection® product monograph. Royal Leamington Spa, Warwickshire; 23 August, 2010.
52. medac GmbH. Epirubicin hydrochloride for injection® product monograph. Hamburg, Germany; 18 August, 2010.
53. Josephine Holmes. Manager Regulatory Affairs, Pharmaceutical Partners of Canada Inc. Personal communication. 12 June, 2009.
54. Berrum-Svennung I, Granfors T, Jahnson S, et al. A single instillation of epirubicin after transurethral resection of bladder tumors prevents only small recurrences. J Urol ; 2008;179(1):101–106
55. van der Meijden AP, Brausi M, Zambon V, et al. Intravesical instillation of epirubicin, bacillus Calmette-Guerin and bacillus Calmette-Guerin plus isoniazid for intermediate and high risk Ta, T1 papillary carcinoma of the bladder: a European Organization for Research and Treatment of Cancer genito-urinary group randomized phase III trial. Journal of Urology. ; 2001;166(2):476–81
56. Rajala P, Liukkonen T, Raitanen M, et al. Transurethral resection with perioperative installation of interferon-alpha or epirubicin for the prophylaxis of recurrent primary superficial bladder cancer : a prospective randomized multicenter study--FinnBladder III. Journal of Urology ; Sep, 1999;161(4):1133–1136
57. American Urological Association: Bladder Cancer Clinical Guideline Update Panel. Guideline for the Management of Nonmuscle Invasive Bladder Cancer: (Stages Ta,T1, and Tis): 2007 Update. : American Urological Association, Education and Research Inc.; 2007, updated Feb 12 , 2014.
58. Australia and New Zealand Urological Nurses Society (ANZUNS) Inc. Clinical Guidelines: Instillation of Intravesical Solutions. Trish White ed. : Australia and New Zealand Urological Nurses Society (ANZUNS) Inc; April , 2012.
59. BC Cancer Agency Breast Tumour Group. (BRAJFEC) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide. Vancouver, British Columbia: BC Cancer Agency; 2005.
60. BC Cancer Agency Breast Tumour Group. (BRAJCEF) BCCA Protocol summary for Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil . Vancouver, British Columbia: BC Cancer Agency; 2005.
61. BC Cancer Agency Breast Tumour Group. (BRINFCEF) BCCA Protocol Summary of Therapy for Inflammatory Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil. Vancouver, British Columbia: BC Cancer Agency; 2005.
62. BC Cancer Agency Breast Tumour Group. (BRLACEF) BCCA Protocol Summary of Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil. Vancouver, British Columbia: BC Cancer Agency; 2005.
63. BC Cancer Agency Breast Tumour Group. (BRAJCEFG) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF). Vancouver, British Columbia: BC Cancer Agency; 2005.
64. BC Cancer Agency Breast Tumour Group. (BRINFCEFG) BCCA Protocol Summary of Therapy for Inflammatory Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF). Vancouver, British Columbia: BC Cancer Agency; 2005.
65. BC Cancer Agency Breast Tumour Group. (BRLACEFG) BCCA Protocol Summary of Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF). Vancouver, British Columbia: BC Cancer Agency; 2005.
66. Zamorano JL, Lancellotti P, Rodriguez Muñoz D:,V., et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines. (The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC)). Eur Heart J ; 2016;37(16):2768–2801
67. Senkus E, Jassem J. Cardiovascular effects of systemic cancer treatment. Cancer Treat Rev ; November 9, 2010:1–12
68. Curigliano G, Cardinale D, Suter T, et al. Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines. Ann Oncol ; 2012;23(Suppl 7):vii 155–vii 166

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