Pharmacy FAQ

Documentation for Cumulative Doses of Anthracyclines and Bleomycin

Q: Why and how should we document cumulative doses of anthracylines and bleomycin?

Anthracyclines, which include DAUNOrubicin, DOXOrubicin (including pegylated liposomal), epirubicin, IDArubicin and the anthracenedione mitoxantrone, can all increase the risk of cardiac toxicity. This is thought to be caused by damage to the myocardial tissue by highly reactive free radicals. Cardiotoxicity manifests as early (acute) or late (delayed) effects. Early toxic effects, which are not dose related, range from mild changes in ECG to life-threatening arrhythmias and may even occur after one dose of the treatment. Delayed cardiotoxic effects are dose-related and may present as symptomatic congestive heart failure (CHF) or decreased left ventricular ejection fraction (LVEF) a year or more after treatment is completed. Changes in LVEF are related to the total cumulative dose, are irreversible and refractory to medical therapy.

A high cumulative dose as well as previous therapy with other anthracyclines, anthracenediones and other cardiotoxic drugs may increase the risk of cardiotoxicity following anthracycline therapy. Caution should be exercised if patient had previous or is on concurrent therapy with other cardiotoxic drugs such as trastuzumab, cyclophosphamide, etoposide and mitomycin. In addition, other factors such as old age, mediastinal (particularly left-sided thoracic) radiation and hypertensive cardiomegaly may also increase this risk. Therefore, it is important to record a patient's lifetime doses of anthracyclines to minimize the risk of cardiotoxicity.

The doxorubicin monograph in the Cancer Drug Manual contains information on anthracycline cardiotoxicity, monitoring thresholds and conversion factors. Pharmacists may be asked to convert cumulative dose from one anthracycline to another. The use of alternative anthracyclines, such as epirubicin or liposomal doxorubicin, or a change in administration frequency from every 3 weeks to a lower weekly dose, can reduce the risk of cardiotoxicity. For patients who have reached a cumulative dose of 300 mg/m² doxorubicin equivalent, therapy with the cardio-protective agent dexrazoxane can be considered. For more information on dexrazoxane, please refer to the dexrazoxane Pharmacy FAQ.

The table below provides a guide for the cumulative dose thresholds at which to start cardiac monitoring. Monitoring should start at a lower threshold if the patient has cardiac and other risk factors.

Table 1. Recommended Conversion Factors, Monitoring Thresholds and Cumulative Doses for Anthracyclines

Drug	Suggested Conversion Factor to Doxorubicin dose	Suggested Monitoring Threshold	Suggested Maximum Cumulative Lifetime Dose	Comments
DAUNOrubicin	x 0.5-0.83	450 mg/m²	900 mg/m²	Reduce cumulative dose to 400-450 mg/m² if other risk factors
DOXOrubicin	x 1	300 mg/m²	450-500 mg/m²	Reduce cumulative dose to 400-450 mg/m² if other risk factors
Liposomal DOXOrubicin	Not Available	400 mg/m² (if previous anthracycline) 700 mg/m² (if no previous anthracycline)	Unknown	Evaluate LVEF when cumulative dose of other anthracyclines is 450 mg/m² prior to starting liposomal doxorubicin
Epirubicin	x 0.5-0.67	600 mg/m²	900 mg/m²	Caution in elderly when cumulative dose > 500 mg/m²
IDArubicin	x 2-5	150 mg/m²	IV = 160 mg/m² PO = 400 mg/m²	Not available
MitoXANTHRONE	x 2.2-4	140 mg/m²	140 mg/m²	Reduce cumulative dose to 100 mg/m² if other risk factors

Adapted from reference numbers 1 and 2

A cumulative dose record for all anthracyclines and bleomycin is kept either electronically (if on Cerner system), or on a paper document located in the patient's BC Cancer chart. See examples of manual and electronic dose records below:

Figure 1. Example table for manual recording of doses

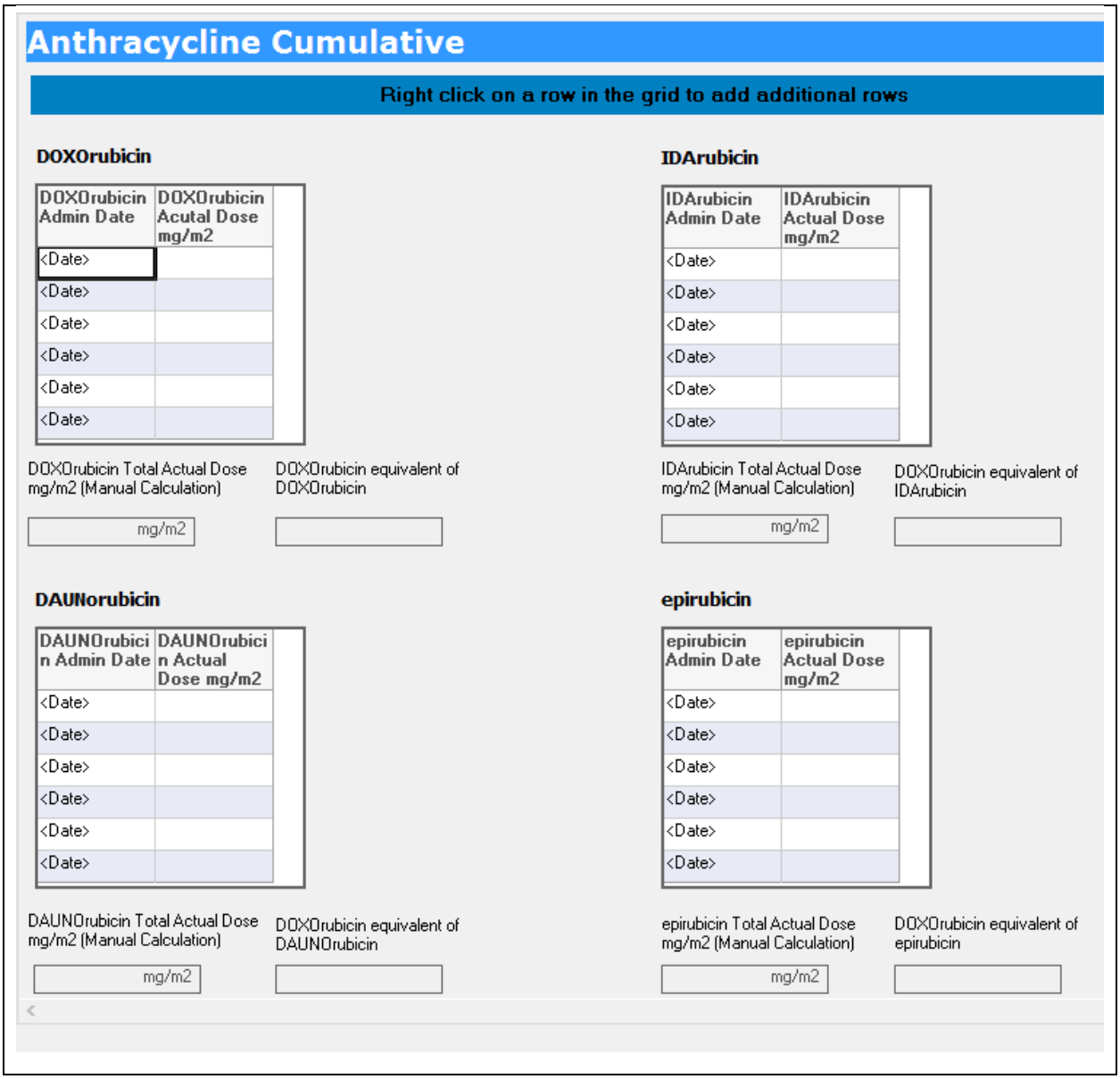
CUMULATIVE DOSES *of* ANTHRACYCLINES *and* BLEOMYCIN

ANTHRACYCLINE _____

BLEOMYCIN _____

DATE	DOSE	TOTAL DOSE	BSA	CUMULATIVE DOSE/m²

Figure 2. Anthracycline cumulative dose record as shown in Cerner

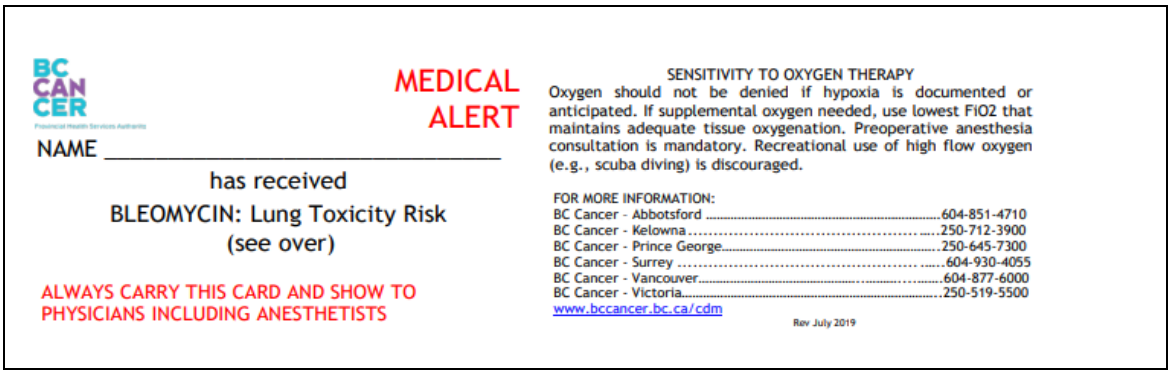


The dose of anthracycline is added at each cycle and the cumulative dose/m² is manually calculated based on the most recent BSA. When the patient is getting close to the monitoring threshold (eg. 300 mg/m² for doxorubicin) the physician should be alerted, unless it is the patient's last cycle. The cumulative dose of pegylated liposomal doxorubicin is also recorded.

Bleomycin is another agent where pharmacists keep a record of cumulative doses. The most serious side effects of bleomycin are respiratory and can occur in 10% of patients. Bleomycin pulmonary toxicity (BPT) can progress to pulmonary fibrosis and death in 1% of patients. Risk factors for developing BPT include compromised pulmonary and renal function, concomitant chest radiation, concomitant therapy with other cancer drugs (eg., cisplatin, cyclophosphamide, methotrexate, etc.), and a cumulative dose of bleomycin greater than 450 units. Therefore, it is important to maintain a record of the lifetime doses of

bleomycin that a patient receives. At BC Cancer, patients are given a medical alert card to inform other health care providers of lung toxicity risk and sensitivity to oxygen therapy. See the Medical Alert card below:

Figure 3. Bleomycin alert card



BC CANCER

MEDICAL ALERT

NAME _____

has received

BLEOMYCIN: Lung Toxicity Risk

(see over)

ALWAYS CARRY THIS CARD AND SHOW TO PHYSICIANS INCLUDING ANESTHETISTS

SENSITIVITY TO OXYGEN THERAPY

Oxygen should not be denied if hypoxia is documented or anticipated. If supplemental oxygen needed, use lowest FiO2 that maintains adequate tissue oxygenation. Preoperative anesthesia consultation is mandatory. Recreational use of high flow oxygen (e.g., scuba diving) is discouraged.

FOR MORE INFORMATION:

BC Cancer - Abbotsford 604-851-4710
BC Cancer - Kelowna 250-712-3900
BC Cancer - Prince George.....250-645-7300
BC Cancer - Surrey 604-930-4055
BC Cancer - Vancouver.....604-877-6000
BC Cancer - Victoria.....250-519-5500
www.bccancer.bc.ca/cdm

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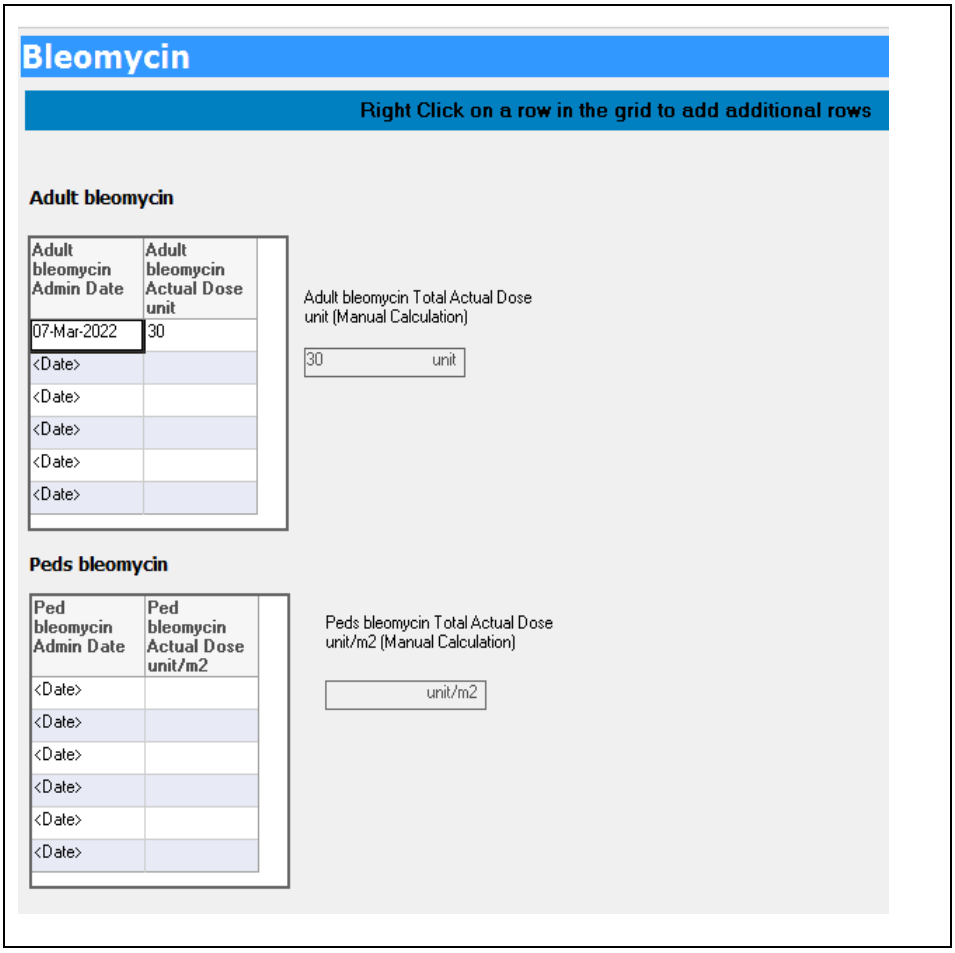
The same paper record as for anthracyclines is used to document the cumulative dose of bleomycin. In institutions using Cerner, documentation of bleomycin doses is carried out electronically.

Figure 4: Bleomycin cumulative dose records as shown in Cerner



Bleomycin

Right Click on a row in the grid to add additional rows

Adult bleomycin

Adult bleomycin Admin Date	Adult bleomycin Actual Dose unit
07-Mar-2022	30
<Date>	
<Date>	
<Date>	
<Date>	
<Date>	

Adult bleomycin Total Actual Dose unit (Manual Calculation)

30 unit

Peds bleomycin

Ped bleomycin Admin Date	Ped bleomycin Actual Dose unit/m2
<Date>	
<Date>	
<Date>	
<Date>	
<Date>	
<Date>	

Peds bleomycin Total Actual Dose unit/m2 (Manual Calculation)

unit/m2

Reference:

1. BC Cancer. Cancer Drug Manual Drug Index [Internet]. Vancouver, BC: BC Cancer Agency [updated continuously; accessed 2022 May 11]. Available from: http://www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual/drug-index.

2. Cardiac toxicity associated with anthracyclines [Internet]. eviQ Cancer Treatments Online. Cancer Institute NSW; 2004 Sept 1 [reviewed 2019 Aug 30; cited 2022 May 9]; 1667 V.4. Available from: https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/cardiovascular/1667-cardiac-toxicity-associated-with-anthracyclin#management

3. Smith LA, Cornelius VR, Plummer CJ, Levitt G, Verrill M, Canney P, Jones A. Cardiotoxicity of anthracycline agents for the treatment of cancer: systematic review and meta-analysis of randomised controlled trials. BMC Cancer. 2010 Jun 29;10:337. doi: 10.1186/1471-2407-10-337.

4. Torti FM, Bristow MR, Howes AE, Aston D, Stockdale FE, Carter SK, Kohler M, Brown BW Jr, Billingham ME. Reduced cardiotoxicity of doxorubicin delivered on a weekly schedule. Assessment by endomyocardial biopsy. Ann Intern Med. 1983 Dec;99(6):745-9. doi: 10.7326/0003-4819-99-6-745.

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