DOSE CONVERSION FOR ANTHRACYCLINE EXPOSURE

Cumulative doses of anthracyclines and anthracenediones may be calculated using the following table to assess the therapeutic exposures during the patient's lifetime.

Agent	Suggested Conversion Factor to DOXOrubicin Dose	Suggested Monitoring Threshold†,¶
DAUNOrubicin	x 0.5[1,2]	450 mg/m^2[18]
DAUNOrubicin liposomal*	Unknown[4,5]	Unknown (tolerated at 1000 mg/m^2)[4,5]
DAUNOrubicin liposomal (in VYXEOS)	Same as conventional DAUNOrubicin[6]	Same as conventional DAUNOrubicin (similar incidence of cardiotoxicity to conventional DAUNOrubicin in "7+3" regimen)[6]
DOXOrubicin Pegylated liposomal	Unknown[7]	Unclear No clear relationship between cumulative dose and cardiotoxicity[5,8] up to > 1000 mg/m2.[11-16] Routine monitoring generally is not indicated[8] but monitoring threshold at 700 mg/m^2[10] and 900 mg/m^2 have been suggested.[8]
DOXOrubicin	x 1[1,2]	300 mg/m^2[17,19]
epirubicin	x 0.67[1]	600 mg/m^2[17,20]
IDArubicin	x 5[1]	150 mg/m^2[21]
mitoXANTRONE	x 10[1,2]	140 mg/m^2[23,24]

*Commercial product not available in Canada, US or EU.

† Dosing based on body weight (mg/kg) may be converted by[3]: daily dose in mg/m^2 = (daily dose in mg)/BSA

¶ Treatment may continue beyond these doses in selected patients, if the clinician has considered the potential risks and benefits. The addition of dexrazoxane may be considered, and monitoring should be increased. Maximum tolerated doses are variable; some patients may tolerate doxorubicin equivalent doses exceeding 1000 mg/m^2 while other patients exhibit symptomatic heat failure at doxorubicin equivalent doses less than 300 mg/m^2.

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References

1. Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 6.0. Children's Oncology Group, October 2023. Available at: www.survivorshipguidelines.org. Accessed 21 March 2024.
2. Feijen EAM, Leisenring WM, Stratton KL, et al. Derivation of anthracycline and anthraquinone equivalence ratios to doxorubicin for late-onset cardiotoxicity. JAMA Oncol 2019;5(6):864-71.
3. BC Children's Hospital. Anthracyline cumulative dose record. Vancouver, BC: March 2021.
4. Gill PS, Espina BM, Muggia F, et al. Phase I/II clinical and pharmacokinetic evaluation of liposomal daunorubicin. J Clin Oncol 1995;13(4):996-1003.
5. DRUGDEX® Evaluations. Daunorubicin Liposome. Merative MICROMEDEX®, 14 November 2022. Available at: www.micromedex.com. Accessed 2 December 2022.
6. Jazz Pharmaceuticals Canada Inc. VYXEOS® product monograph. Mississauga, Ontario; April 28, 2021.
7. Janssen Inc. CAELYX® product monograph. Toronto, Ontario; 2 Jun 2020.
8. 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:vii155-vii166.
9. eviQ. Cardiac toxicity associated with anthracyclines. Cancer Institute NSW, 31 December 2021. Available at www.eviq.org.au. Accessed 6 December 2022.
10. Kesterson JP, Odunsi K, Lele S. High cumulative doses of pegylated liposomal doxorubicin are not associated with cardiac toxicity in patients with gynecologic malignancies. Chemotherapy 2010;56(2):108-111.
11. Rayson D, Suter TM, Jackisch C, et al. Cardiac safety of adjuvant pegylated liposomal doxorubicin with concurrent trastuzumab: a randomized phase II trial. Ann Oncol 2012;23(7):1780-8.
12. Gill SE, Savage K, Wysham WZ, et al. Continuing routine cardiac surveillance in long-term use of pegylated liposomal doxorubicin: Is it necessary? Gynecol Oncol 2013;129(3):544–7.
13. Rabinovich A, Ramanakumar AV, Lau S, Gotlieb WH. Prolonged pegylated liposomal doxorubicin treatment for recurrent pelvic cancers: a feasibility study. Acta Obstet Gynecol Scand 2015;94(7):776–80.
14. Pendlebury A, DeBernardo R, Rose PG. Long-term use of pegylated liposomal doxorubicin to a cumulative dose of 4600 mg/m2 in recurrent ovarian cancer. Anticancer Drugs 2017;28(7):815–7.
15. Yost S, Konal JL, Hoekstra AV. Prolonged use of pegylated liposomal doxorubicin in gynecologic malignancies. Gynecol Oncol Rep 2019;29:89-93.
16. Li XR, Cheng XH, Zhang GN, et al. Cardiac safety analysis of first-line chemotherapy drug pegylated liposomal doxorubicin in ovarian cancer. J Ovarian Res 2022;15(1):96.
17. 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 2007;25(25):3991-4008.
18. Teva Canada Limited. Daunorubicin hydrochloride for injection product monograph. Toronto, Ontario; 19 November 2013.
19. Accord Healthcare Inc. Doxorubicin injection® product monograph. Kirkland, Quebec; 19 November 2018.
20. Pfizer Canada Inc. Epirubicin hydrochloride injection product monograph. Kirkland, Quebec; 6 October 2017.
21. Pfizer Canada Inc. IDARUBICIN® product monograph. Kirkland, Quebec; 19 August 2014.
22. Anderlini P, Benjamin RS, Wong FC, et al. Idarubicin cardiotoxicity: a retrospective study in acute myeloid leukemia and myelodysplasia. J Clin Oncol 1995;13(11):2827-2834.
23. Fresenius Kabi Canada Ltd. Mitoxantrone injection® product monograph. Richmond Hill, Ontario; 28 September 2016.
24. Tannock IF, Osoba D, Stockler MR, et al. Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points. J Clin Oncol 1996;14(6):1756-1764.