

# British Columbia Cancer Agency | POLICY

<b>Title:</b> PHYSICIAN COVERAGE FOR MEDICAL EMERGENCIES DURING DELIVERY OF SELECTED CHEMOTHERAPY DRUGS		<b>Number:</b> III-60
<b>Effective Date:</b> June 2001	<b>Approved By:</b> Provincial Systemic Program Committee	
<b>Revised:</b> 1 Feb 2012		

## Reason for Directive

To ensure safe management of medical emergencies arising during chemotherapy treatments.

## Directive

When the following drugs are given intravenously, a physician must remain on site for the following durations after initiation (i.e., from the start of the infusion) of each treatment (unless otherwise specified):

<b>30 minutes</b>	<b>60 minutes</b>	<b>3 hours</b>	<b>During entire infusion</b>
<ul style="list-style-type: none"> <li>▪ Alemtuzumab</li> <li>▪ Asparaginase</li> <li>▪ Bleomycin</li> <li>▪ Carboplatin</li> <li>▪ Docetaxel</li> <li>▪ Etoposide</li> <li>▪ Paclitaxel</li> <li>▪ Rituximab†</li> <li>▪ Tositumomab</li> </ul>	<ul style="list-style-type: none"> <li>▪ Cetuximab††</li> </ul>	<ul style="list-style-type: none"> <li>▪ Rituximab*</li> </ul>	<ul style="list-style-type: none"> <li>▪ Oxaliplatin</li> <li>▪ Trastuzumab§</li> </ul>

\* First dose only

† Second and subsequent doses

§ For first dose, plus additional 60 min after end of infusion; for second and third doses, plus 30 min after end of infusion. No additional observation period is needed if no reactions after 3 consecutive treatments.

\*\* drugs reviewed for this policy included drugs added to the BC Cancer Agency Benefit List between June 2001 and November 2011, including azacitidine, bevacizumab, bortezomib, panitumumab, pemetrexed, porfimer, temsirolimus, teniposide.

†† 60 minutes following end of first and second infusion, may discontinue observation period if no infusion reactions occur for two consecutive doses.

See Appendix

# British Columbia Cancer Agency | POLICY

<b>Title:</b> PHYSICIAN COVERAGE FOR MEDICAL EMERGENCIES DURING DELIVERY OF SELECTED CHEMOTHERAPY DRUGS		<b>Number:</b> III-60
<b>Effective Date:</b> June 2001	<b>Approved By:</b> Provincial Systemic Program Committee	
<b>Revised:</b> 1 Feb 2012		

Page 2 of 4

## APPENDIX

Data source: manufacturer's product monographs and MEDLINE search combining MeSHs of "drug hypersensitivity" or "immediate hypersensitivity" with "antineoplastic agents", limited to humans and English language. The threshold for inclusion was largely based on the emphasis placed by the manufacturer, although in some cases (e.g., oxaliplatin) the literature report may also be pivotal. Length of physician coverage takes into account of the likely documented onset of reactions and the usual infusion time.

<i>Drug</i>	<i>Toxicity</i>	<i>Onset</i>	<i>Incidence</i>
<b>alemtuzumab</b> <sup>1</sup>	infusion reactions (hypotension, rigors, fever, shortness of breath, bronchospasm, chills, rash)	not defined	26-96% (severe 9-16%)
<b>asparaginase</b> <sup>2-4</sup>	hypersensitivity reactions	30-60 min	severe 3-32%
<b>bleomycin</b>	hypersensitivity reactions (hypotension, fever, chills, mental confusion, wheezing) <sup>5</sup>	½ - 6 h after first or second dose <sup>6</sup>	1% <sup>5</sup>
<b>cetuximab</b> <sup>7</sup>	infusion reactions (rapid onset of airway obstruction, urticaria, hypotension)	not defined	13-19% (severe 2-5%) <sup>8</sup>
<b>carboplatin</b>	hypersensitivity reactions	usually immediately after start of the infusion; however, there are reports of reactions delayed for several hours <sup>8,9</sup>	2-30% <sup>9-11</sup>
<b>docetaxel</b>	hypersensitivity reactions	a few minutes after start of the infusion <sup>12</sup>	21% (severe 4%) <sup>13</sup>
<b>etoposide</b>	hypersensitivity reactions	<ul style="list-style-type: none"> <li>▪ can be either after only a few milligrams of drug have been infused or up to several hours after administration</li> <li>▪ more often occur while the drug is being infused<sup>14</sup> or within minutes after start of infusion<sup>15</sup></li> </ul>	1-3% <sup>16</sup>
<b>oxaliplatin</b> <sup>17-19</sup>	hypersensitivity reactions	usually within 30 min after start of infusion <sup>19-25</sup> but may occur any time during infusion <sup>18,20,22</sup> ; rarely shortly after end of infusion <sup>19,21,23</sup>	severe 3% <sup>17</sup> (post-marketing reported up to 18%) <sup>18,19</sup>
<b>oxaliplatin</b> <sup>17-19</sup>	pharyngolaryngeal dysesthesia <sup>26,27</sup>	shortly after end of infusion	1-2%

# British Columbia Cancer Agency | POLICY

<b>Title:</b> PHYSICIAN COVERAGE FOR MEDICAL EMERGENCIES DURING DELIVERY OF SELECTED CHEMOTHERAPY DRUGS		<b>Number:</b> III-60
<b>Effective Date:</b> June 2001	<b>Approved By:</b> Provincial Systemic Program Committee	
<b>Revised:</b> 1 Feb 2012		

<i>Drug</i>	<i>Toxicity</i>	<i>Onset</i>	<i>Incidence</i>
<b>paclitaxel</b>	hypersensitivity reactions	53% occur within 2-3 min after start of infusion and 78% occur within 10 min <sup>28</sup>	41% (severe 2%)
<b>panitumumab</b>	hypersensitivity and infusion reactions (mild chills, fever, dyspnea) <sup>38</sup>	within 24 h <sup>39</sup>	3-4% (severe 1%) <sup>39</sup>
<b>rituximab</b>	infusion-related hypersensitivity (rash, urticaria, fever, chills, bronchospasm, angioedema, flushing, hypotension, rhinitis, nausea, asthenia, headache) <sup>29,30</sup>	< 1–2 h after start of first infusion <sup>31</sup>	up to 80% (severe 7%)
<b>temsirolimus</b>	hypersensitivity and infusion reactions (loss of consciousness, hypotension, chest pain, dyspnea, apnea) <sup>36</sup>	usually with initial dosing and within minutes of starting the infusion <sup>36</sup>	9% <sup>37</sup>
<b>teniposide</b>	Hypersensitivity reactions (chills, fever, tachycardia, dyspnea, bronchospasm, hypotension or hypertension) <sup>42</sup>	not defined	1-5% <sup>41</sup>
<b>tositumomab</b> <sup>32</sup>	hypersensitivity reactions, including anaphylaxis	not defined	severe 6%
<b>trastuzumab</b>	infusion reactions (fever, chills)	usually occurs during infusion <sup>33</sup>	36-39% <sup>34,35</sup>

## References:

- Berlex. CAMPATH® product monograph. Montville, NJ, USA; July 2005.
- Graham ML. Pegaspargase: a review of clinical studies. *Adv Drug Deliv Rev* 2003;55(10):1293-302.
- Bryant R. Use of a protocol to minimize hypersensitivity reactions with asparaginase administration. *J Intraven Nurs* 2001;24(3):169-73.
- Asselin BL. The three asparaginases. Comparative pharmacology and optimal use in childhood leukemia. *Adv Exp Med Biol* 1999;457:621-9.
- McEvoy GK, editor. AHFS 2002 Drug Information. Bethesda, Maryland: American Society of Health-System Pharmacists, Inc.; 2004.
- Alcorn BT. Bleomycin hypersensitivity: a case report. *Can J Hosp Pharm* 1980;33(3):92-3.
- ImClone Systems Incorporated, Bristol-Myers Squibb Company. ERBITUX® product monograph. Princeton, NJ, USA; May 2010.
- Thomas M. Cetuximab: adverse event profile and recommendations for toxicity management. *Clin J Oncol Nurs*. 2005; 9 (3): 322-328.
- Weidmann B, Mulleneisen N, Bojko P, et al. Hypersensitivity reactions to carboplatin. Report of two patients, review of the literature, and discussion of diagnostic procedures and management. *Cancer* 1994;73(8):2218-22.
- Markman M, Kennedy A, Webster K, et al. Clinical features of hypersensitivity reactions to carboplatin. *J Clin Oncol* 1999;17(4):1141-85.
- Schiavetti A, Varrasso G, Maurizi P, et al. Hypersensitivity to carboplatin in children. *Medical & Pediatric Oncology* 1999;32(3):183-5.
- Yu DY, Dahl GV, Shames RS, et al. Weekly dosing of carboplatin with vincristine increases risk of allergy in children with brain tumors. *Proc Am Soc Clin Oncol* 2000;19:abstract 2311-Proc Am Soc Clin Oncol 2000;abstract 2311.
- Tankanow RM. Docetaxel: a taxoid for the treatment of metastatic breast cancer. *Am J Health Syst Pharm* 1998;55(17):1777-91.
- Aventis Pharma Inc. TAXOTERE® product monograph. Saint-Laurent: Québec; 26 April 1999.
- Weiss RB. Hypersensitivity reactions. *Seminars in Oncology* 1992;19(5):458-77.
- Hoetelmans RM, Schornagel JH, ten Bokkel Huinink WW, et al. Hypersensitivity reactions to etoposide. *Ann Pharmacother* 1996;30(4):367-71.
- Siderov J, Prasad P, De Boer R, et al. Safe administration of etoposide phosphate after hypersensitivity reaction to intravenous etoposide. *Br J Cancer* 2002;86(1):12-3.

# British Columbia Cancer Agency | POLICY

<b>Title:</b> PHYSICIAN COVERAGE FOR MEDICAL EMERGENCIES DURING DELIVERY OF SELECTED CHEMOTHERAPY DRUGS	<b>Number:</b> III-60
<b>Effective Date:</b> June 2001	<b>Approved By:</b> Provincial Systemic Program Committee
<b>Revised:</b> 1 Feb 2012	

Page 4 of 4

18. Sanofi-Synthelabo. ELOXATIN®: Summary of product characteristics. New York, NY, USA; 9 August 2002.
19. Gowda A, Goel R, Berdzik J, et al. Hypersensitivity Reactions to oxaliplatin: incidence and management. *Oncology (Huntingt)* 2004;18(13):1671-5; discussion 6.
20. Brandi G, Pantaleo MA, Galli C, et al. Hypersensitivity reactions related to oxaliplatin (OHP). *Br J Cancer* 2003;89(3):477-81.
21. Bonosky K, Miller R. Hypersensitivity reactions to oxaliplatin: what nurses need to know. *Clin J Oncol Nurs* 2005;9(3):325-30.
22. Meyer L, Zuberbier T, Worm M, et al. Hypersensitivity reactions to oxaliplatin: cross-reactivity to carboplatin and the introduction of a desensitization schedule. *J Clin Oncol* 2002;20(4):1146-7.
23. Lenz G, Hacker UT, Kern W, et al. Adverse reactions to oxaliplatin: a retrospective study of 25 patients treated in one institution. *Anticancer Drugs* 2003;14(9):731-3.
24. Thomas RR, Quinn MG, Schuler B, et al. Hypersensitivity and idiosyncratic reactions to oxaliplatin.[see comment]. *Cancer* 2003;97(9):2301-7.
25. Bhargava P, Gammon D, McCormick MJ. Hypersensitivity and idiosyncratic reactions to oxaliplatin.[comment]. *Cancer* 2004;100(1):211-2.
26. Maindrault-Goebel F, Andre T, Tournigand C, et al. Allergic-type reactions to oxaliplatin: Retrospective analysis of 42 patients. *Eur J Cancer* 2005;41(15):2262-7.
27. Wiseman LR, Adkins JC, Plosker GL, et al. Oxaliplatin: a review of its use in the management of metastatic colorectal cancer. *Drugs Aging* 1999;14(6):459-75.
28. Sanofi-Synthelabo. Eloxatin: Summary of product characteristics (Europe). France; 1 October 1999.
29. Bernstein BJ. Docetaxel as an alternative to paclitaxel after acute hypersensitivity reactions. *Ann Pharmacother* 2000;34(11):1332-5.
30. Hoffmann-LaRoche. RITUXAN® product monograph. Mississauga, Ontario; 21 June, 2000.
31. McLaughlin P, Hagemester FB, Grillo-Lopez AJ. Rituximab in indolent lymphoma: the single-agent pivotal trial. *Semin Oncol* 1999;26(5 Suppl 14):79-87.
32. Onrust SV, Lamb HM, Balfour JA. Rituximab. *Drugs* 1999;58(1):79-88; discussion 9-90.
33. GlaxoSmithKline Inc. BEXXAR™ product monograph. Montville, NJ, USA; 18 August 2005.
34. Cobleigh MA, Vogel CL, Tripathy D, et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. *J Clin Oncol* 1999;17(9):2639-48. =
35. Hoffmann-LaRoche. HERCEPTIN® product monograph - important drug warning. Mississauga, Ontario; 4 May, 2000.
36. Hoffmann-LaRoche. HERCEPTIN® product monograph. Mississauga, Ontario; 26 June, 2000.
37. Rose BD editor. Temsirolimus. UpToDate 16.3 ed. Waltham, Massachusetts: UpToDate®; 2008.
38. Wyeth Canada. TORISEL® product monograph. Montreal, Canada; 16 October 2008.
39. Amgen Canada. VECTIBIX® product monograph. Mississauga, Ontario; 5 March 2009.
40. McEvoy GK, editor. AHFS 2008 Drug Information. Bethesda, Maryland: American Society of Health-System Pharmacists, Inc. p. 1189-1191.
41. AHFS Drug Information® (database on the Internet). Teniposide. Lexi-Comp Inc., March 2011
42. Bristol-Myers Squibb Canada. VUMON® product monograph. St. Laurent, Quebec; 26 October 2004.