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):

<table>
<thead>
<tr>
<th>30 minutes</th>
<th>60 minutes</th>
<th>3 hours</th>
<th>During entire infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>alemtuzumab</td>
<td>cetuximab†</td>
<td>riTUXimab*</td>
<td>bendamustine</td>
</tr>
<tr>
<td>asparaginase</td>
<td></td>
<td></td>
<td>brentuximab</td>
</tr>
<tr>
<td>bleomycin</td>
<td></td>
<td></td>
<td>oBiNutzumab</td>
</tr>
<tr>
<td>cabazitaxel</td>
<td></td>
<td></td>
<td>oxaliplatin</td>
</tr>
<tr>
<td>CARBOplatin</td>
<td></td>
<td></td>
<td>PERTuzumab§</td>
</tr>
<tr>
<td>DOCEtaxel</td>
<td></td>
<td></td>
<td>trastuzumab§</td>
</tr>
<tr>
<td>etoposide</td>
<td></td>
<td></td>
<td>trastuzumab emtansine§</td>
</tr>
<tr>
<td>PACLitaxel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>riTUXimab†</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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.
‡ 60 minutes following end of first and second infusion, may discontinue observation period if no infusion reactions occur for two consecutive doses.
**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) literature reports may also be pivotal. Length of physician coverage takes into account of the likely documented onset of reactions and the usual infusion time.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Toxicity</th>
<th>Onset</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>alemtuzumab1</td>
<td>infusion reactions (hypotension, rigors, fever, shortness of breath, bronchospasm, chills, rash)</td>
<td>not defined</td>
<td>26-96% (severe 9-16%)</td>
</tr>
<tr>
<td>asparaginase2-4</td>
<td>hypersensitivity reactions</td>
<td>30-60 min</td>
<td>severe 3-32%</td>
</tr>
<tr>
<td>bendamustine5,6</td>
<td>infusion reactions (fever, chills, pruritus, shortness of breath, hypotension, cyanosis, tachycardia, rash; rarely, severe anaphylactic and anaphylactoid reactions)</td>
<td>during or directly after drug administration</td>
<td>5% (severe 1%)</td>
</tr>
<tr>
<td>bleomycin7,8</td>
<td>hypersensitivity reactions</td>
<td>30 minutes to 6 hours after first or second dose</td>
<td>1%</td>
</tr>
<tr>
<td>brentuximab9,10</td>
<td>infusion reactions (chills, nausea, dyspnea, pruritus, pyrexia, cough, wheezing, difficulty breathing, hives, itching, swelling)</td>
<td>immediate or delayed up to 2 days</td>
<td>12%</td>
</tr>
<tr>
<td>cabazitaxel11</td>
<td>hypersensitivity reactions</td>
<td>not defined</td>
<td>severe &lt;1%</td>
</tr>
<tr>
<td>cetuximab12,13</td>
<td>infusion reactions (rapid onset of airway obstruction, urticaria, hypotension)</td>
<td>not defined</td>
<td>13-19% (severe 2-5%)</td>
</tr>
<tr>
<td>CARBOplatin14-17</td>
<td>hypersensitivity reactions</td>
<td>usually immediately after start of the infusion; may delay for several hours</td>
<td>2-30%</td>
</tr>
<tr>
<td>DOCEtaxel18,19</td>
<td>hypersensitivity reactions</td>
<td>a few minutes after start of the infusion</td>
<td>21% (severe 4%)</td>
</tr>
<tr>
<td>etoposide14,20,21</td>
<td>hypersensitivity reactions</td>
<td>usually during infusion or within minutes after start of infusion; may occur after only a few milligrams have been infused or up to several hours after administration</td>
<td>1-3%</td>
</tr>
</tbody>
</table>
**Drug** | **Toxicity** | **Onset** | **Incidence**
--- | --- | --- | ---
**oBInutuzumab** | infusion reactions (nausea, vomiting, chills, hypotension, pyrexia, dyspnea, flushing, hypertension, headache, tachycardia, diarrhea)\(^{22}\) | not well defined, but probably within 1-2 hours after start of infusion of first dose and more than 5 hours after start of infusion of second dose\(^{23,24}\) | 53% (severe 17%)\(^{25}\)

**oxaliplatin\(^{26-36}\)** | hypersensitivity reactions | usually within 30 min after start of infusion but may occur any time during infusion; rarely shortly after end of infusion | severe 3% (up to 18%)

 | pharyngolaryngeal dysesthesia | shortly after end of infusion | 1-2%

**PACLitaxel\(^{37}\)** | hypersensitivity reactions | 53% within 2-3 min after start of infusion and 78% within 10 min | 41% (severe 2%)

**PERTuzumab** | infusion reactions (fever, chills, fatigue, headaches, asthenia, hypersensitivity, vomiting) | not defined | 11%, (severe 2-5%)

**ritTUXimab\(^{38-40}\)** | infusion-related hypersensitivity (rash, urticaria, fever, chills, bronchospasm, angioedema, flushing, hypotension, rhinitis, nausea, asthenia, headache)\(^{19,30}\) | < 1–2 h after start of first infusion\(^{31}\) | up to 80% (severe 7%)

**trastuzumab** (HERCEPTIN)\(^{41-43}\) | infusion reactions (fever, chills) | usually during infusion | 36-39%

**trastuzumab emtansine** (KADCYLA)\(^{44}\) | infusion reactions (flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, tachycardia) | not defined | 1%

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**References:**
5. Lundbeck Canada Inc. TREANDA® product monograph. Montreal, Quebec; 22 August 2012.
44. Genentech Inc. KADCYLA® full prescribing information. South San Francisco, CA, USA; 22 February 2013.