**Title:** DRUG REACTION MANAGEMENT--PHYSICIAN COVERAGE DURING DELIVERY OF SELECTED SYSTEMIC THERAPY DRUGS

**Number:** III-60

**Effective Date:** June 2001

**Revised:** 25Jan2018

**Approved By:** Provincial Systemic Program Committee

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**Reason for Directive**

To ensure safe management of drug reactions arising during chemotherapy treatments.

**Directive**

When the following drugs are given, 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>alemuzumab</td>
<td>cetuximab‡</td>
<td>riTUXimab*</td>
<td>bendamustine</td>
</tr>
<tr>
<td>asparaginase</td>
<td></td>
<td></td>
<td>blinatumomab§</td>
</tr>
<tr>
<td>bleomycin</td>
<td></td>
<td></td>
<td>brentuximab vedotin</td>
</tr>
<tr>
<td>cabazitaxel</td>
<td></td>
<td></td>
<td>oBINutuzumab</td>
</tr>
<tr>
<td>CARBOplatin</td>
<td></td>
<td></td>
<td>oxaliplatin</td>
</tr>
<tr>
<td>DOCEtaxel</td>
<td></td>
<td></td>
<td>PERTuzumab¶</td>
</tr>
<tr>
<td>etoposide</td>
<td></td>
<td></td>
<td>trastuzumab¶</td>
</tr>
<tr>
<td>PACLitaxel</td>
<td></td>
<td></td>
<td>trastuzumab emtansine¶</td>
</tr>
<tr>
<td>riTUXimab†</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* First IV infusion dose only; physician does not need to be on site for subcutaneous injection.
† Second and subsequent doses
‡ 60 minutes following end of first and second infusion, may discontinue observation period if no infusion reactions occur for two consecutive doses.
§ Hospitalization recommended at a minimum for the first 9 days of cycle 1 and first 2 days of cycle 2. Subsequent cycles may be started as an outpatient.
¶ 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.
### 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>alemtuzumab</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>asparaginase</td>
<td>hypersensitivity reactions</td>
<td>30-60 min</td>
<td>severe 3-32%</td>
</tr>
<tr>
<td>bendamustine</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>bleomycin</td>
<td>hypersensitivity reactions</td>
<td>30 minutes to 6 hours after first or second dose</td>
<td>1%</td>
</tr>
<tr>
<td>blinatumomab</td>
<td>cytokine release syndrome</td>
<td>2 days after start of infusion</td>
<td>11% (severe 1%)</td>
</tr>
<tr>
<td>Brentuximab vedotin</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>cabazitaxel</td>
<td>hypersensitivity reactions</td>
<td>not defined</td>
<td>severe &lt;1%</td>
</tr>
<tr>
<td>cetuximab</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>CARBOplatin</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>DOCEtaxel</td>
<td>hypersensitivity reactions</td>
<td>a few minutes after start of the infusion</td>
<td>21% (severe 4%)</td>
</tr>
<tr>
<td>etoposide</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>
<tr>
<td>oBINutuzumab</td>
<td>infusion reactions (nausea, vomiting, chills, hypotension, pyrexia, dyspnea, flushing, hypertension, headache, tachycardia, diarrhea)</td>
<td>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</td>
<td>53% (severe 17%)</td>
</tr>
</tbody>
</table>
**Drug** | **Toxicity** | **Onset** | **Incidence**
---|---|---|---
Oxaliplatin | 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 | Shorty after end of infusion | 1-2%
Paclitaxel | Hypersensitivity reactions | Usually within 3-5 min after start of infusion, 78% within 10 min | 41% (severe 2%)
Perituzumab | Infusion reactions (fever, chills, fatigue, headaches, asthenia, hypersensitivity, vomiting) | Not defined | 11%, (severe 2-5%)
Rituximab | Infusion-related hypersensitivity (rash, urticaria, fever, chills, bronchospasm, angioedema, flushing, hypotension, rhinitis, nausea, asthenia, headache) | < 1-2 h after start of first infusion | Up to 80% (severe 7%)
Trastuzumab (Herceptin) | Infusion reactions (fever, chills) | Usually during infusion | 36-39%
Trastuzumab emtansine (Kadcyla) | Infusion reactions (flushing, chills, pyrexia, dyspnea, hypotension, wheezing, bronchospasm, tachycardia) | Not defined | 1%

References:
5. Lundbeck Canada Inc. TREANDA® product monograph. Montreal, Quebec; 22 August 2012.
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