Definition of Infusion-Related Reactions
An adverse sign or symptom occurring during drug infusion or within the first day of drug administration. Infusion-related reactions include hypersensitivity or allergic reactions such as anaphylaxis (antibody mediated) or anaphylactoid reactions (not antibody mediated), such as cytokine-release syndrome.\textsuperscript{1-6} Reactions may include urticaria, dyspnea, bronchospasm, angioedema, hypotension, tachycardia, back or abdominal discomfort/pain. Occasionally cardiorespiratory arrest may occur.

TREATMENT\textsuperscript{7-15}

1. General Management: It is recommended that patients are assessed by a physician if having a reaction requiring the administration of medications or as the patient condition warrants. Two interim preprinted physician orders are available for internal use at BC Cancer (H:\EVERYONE\SYSTEMIC\Chemo\Protocol\Interim Protocol):
   a. Preprinted Order A for immediate management, including the infusion rate for resumption of infusion for selected drugs (PACLitaxel, DOCEtaxel, rituximab, daratumumab).
   b. Preprinted Order B for subsequent cycle administration of the drug after an infusion reaction.
<table>
<thead>
<tr>
<th>Infusion-related reactions</th>
<th>Management</th>
</tr>
</thead>
</table>
| **Moderate** e.g., moderate rash, flushing, pruritis, mild dyspnea, chest discomfort, abdominal discomfort, lower back pain, mild hypotension | **Immediate Management – Use Preprinted Order A**  
- Stop infusion.  
- Give diphenhydRAMINE 50 mg IV push and/or hydrocortisone sodium succinate 100 mg IV push per physician orders.  
- After recovery of symptoms, resume infusion at a rate per protocol. If no direction in protocol consider resuming at 25% of previous rate for at least 5 minutes, 50% for at least 5 minutes, 75% for at least 5 minutes and then full rate if no reaction.  
- Depending on severity of reaction, may increase to full rate at physician's discretion. |

| **Severe (potentially life threatening)** i.e., to be used if reaction escalates (e.g., one or more of respiratory distress requiring treatment, angioedema, hypotension requiring therapy) | **Immediate Management – Use Preprinted Order A**  
- Stop infusion and do not restart.  
- Give epinephrine 0.5 mg* intramuscularly STAT. Repeat epinephrine at 5 minute intervals twice more as needed (i.e., if breathing becomes more laboured or level of consciousness decreases). Note: Administer a maximum of three doses of epinephrine.  
- Give diphenhydRAMINE 50 mg IV push and/or hydrocortisone sodium succinate 100 mg IV push per physician orders.  
- Oxygen if needed for dyspnea (see below).  
- Normal saline if needed for hypotension (see below).  
- Bronchodilators if indicated (see below).  
- Either permanently discontinue the drug that caused the reaction or attempt to retreat on another occasion after premedication (see prophylaxis section) and using Preprinted Order B for a slower infusion rate.  
- **Initiate Emergency Response System appropriate for facility if patient condition warrants.** |

*Note: epinephrine 1:1,000 = 1 mg/mL and epinephrine 1:10,000 = 1 mg/10 mL*
2. **Hypotension:** Administer normal saline to maintain blood pressure per physician orders (e.g., 300 mL/h).

3. **Dyspnea:** Administer oxygen to maintain oxygen saturations per physician orders and/or provide patient comfort.

4. **Bronchospasm:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline (See appendix)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In Order of Preference:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>salbutamol (inhaler)*</td>
<td>200 mcg</td>
<td>2 puffs (100 mcg x 2) via aerosol chamber</td>
</tr>
<tr>
<td>salbutamol (nebules)</td>
<td>5 mg</td>
<td>by nebulizer per facility standard (must follow PPE requirements‡)</td>
</tr>
<tr>
<td>ipratropium / salbutamol§</td>
<td>20 mcg / 100 mcg</td>
<td>1 puff via aerosol chamber</td>
</tr>
<tr>
<td>ipratropium (inhaler)†</td>
<td>40 mcg</td>
<td>2 puffs (20 mcg x 2) via aerosol chamber</td>
</tr>
<tr>
<td>ipratropium (nebules) (ATROVENT®)</td>
<td>0.5 mg</td>
<td>by nebulizer per facility standard (must follow PPE requirements‡)</td>
</tr>
</tbody>
</table>

| **If severe bronchospasm:**         |                       |                                                                                         |
| salbutamol                          |                       | Select one formulation of salbutamol AND one formulation of ipratropium listed above, and follow dosing and administration guideline |
| ipratropium (ATROVENT®)             |                       |                                                                                         |
| ipratropium / salbutamol§           | 20 mcg / 100 mcg      | 1 puff via aerosol chamber                                                            |

* Before administration, prime the device by shaking well and releasing 4 puffs into the air, away from the face.
§ Before administration, prime the device by releasing 1 puff into the air, away from the face, until a soft mist is visible. Then, repeat the process 3 more times. COMBIVENT RESPIMAT® does not need to be shaken.
† Before administration, prime the device by shaking well and releasing 2 puffs into the air, away from the face.
‡ See Procedure: Application of COVID-19 Personal Protective Equipment (PPE) Framework for BC Cancer

**PROPHYLAXIS**
- Determine if the drug or route is essential or if an alternative can be used (e.g., substitute DOCEtaxel for PACLitaxel, CISplatin for CARBOplatin, oral etoposide for parenteral etoposide).
- If the drug or route is essential, pre-treat according to the guidelines for prophylaxis of infusion-related reactions in the protocol by which the patient is being treated.
- If no protocol available consider the following:
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>dexamethasone</td>
<td>20 mg given 12 h and 6 h pre-chemotherapy</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>AND/OR</td>
<td></td>
</tr>
<tr>
<td>diphenhydrAMINE</td>
<td>50 mg given 30 min pre-chemotherapy</td>
<td>IV in 50 mL NS over 20 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(compatible 3 h when mixed in bag)</td>
</tr>
<tr>
<td>ranitidine</td>
<td>50 mg given 30 min pre-chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

References:
Appendix. Instructions for administration of mdi in combination with aerosol chamber
(Adapted from Asthma Canada – How to Use Your Inhaler)

1. Shake the inhaler well before use (as per footnotes in Dosing and Administration table).
2. Remove the cap from the inhaler.
3. Insert the inhaler into the aerosol chamber.
4. Instruct patient to breathe out, away from the aerosol chamber.
5. Bring the aerosol chamber to patient’s mouth, and instruct the patient to put the mouthpiece between their teeth and close their lips around the mouthpiece.
6. Press the top of the inhaler once.
7. Instruct patient to breathe in slowly, if possible, until a full breath is taken. If you hear a whistle sound, the patient is breathing in too fast.
8. Instruct the patient to hold their breath for several seconds, if possible, then breathe out slowly.