

### To Whom It May Concern:

This patient is receiving a **Bispecific Antibody** at BC Cancer and is at risk of **Cytokine Release Syndrome (CRS)** and **Neurotoxicity** (specifically immune effector cell-associated neurotoxicity syndrome – ICANS) which can be **life threatening** and require **urgent management**.

Toxicities associated with bispecific antibodies are different from those seen with standard chemotherapies or targeted therapies, as well as other types of immunotherapy (i.e. checkpoint inhibitors). Bispecific antibodies can cause over activation and dysregulation of the immune system, with a large number of activated white blood cells releasing inflammatory cytokines. **They may also increase the risk of infection despite normal blood counts.**

**CRS** is an acute systemic inflammatory reaction characterized by fever, hypotension, hypoxia and multiorgan dysfunction. **ICANS** is a neurological syndrome that ranges from mild confusion to speech disturbances, seizures, motor weakness, and rarely cerebral edema or coma. CRS and ICANS may occur together or independently.

**For more details, see BC Cancer CRS and ICANS management guidelines (SCCRS, SCICANS) at:**

<http://www.bccancer.bc.ca/health-professionals/clinical-resources/chemotherapy-protocols/supportivecare>

Adverse events can occur during or following treatment and can be life threatening. They can present with mild symptoms that lead to rapid clinical deterioration. **Fever alone may represent Grade 1 CRS.** Treatment, such as tocilizumab, may be required for Grade 2 or higher.

### CRS Grading

Grade	Fever	Hypotension	and/or Hypoxia
1	$\geq 38^{\circ}\text{C}$	None	None
2	$\geq 38^{\circ}\text{C}$	Responsive to IV fluids	Requiring $\leq 6\text{ L/min}$
3	$\geq 38^{\circ}\text{C}$	Requiring a vasopressor with or without vasopressin	Requiring $> 6\text{ L/min}$
4	$\geq 38^{\circ}\text{C}$	Requiring multiple vasopressors (with or without vasopressin)	Requiring CPAP, BIPAP or intubation

Management of bispecific toxicities necessitates prompt coordination with a medical oncologist and potential initiation of high-dose corticosteroids and other treatments (i.e. tocilizumab). It may require other supportive therapies or referral to the Intensive Care Unit if severe. If you suspect your patient is presenting with a toxicity secondary to their bispecific antibody, **please contact the patient's medical oncologist/hematologist** directly or, if after hours, contact the on-call physician, or as per your local centre's process (next page).

<b>BC CANCER CENTRES</b>	<b>For PATIENTS: Provincial/Telephone Nurse Lines</b>
<b>Abbotsford Prince George Surrey Vancouver Victoria</b>	<b>Call the 24/7 Provincial Nurse Line (PNL): 1-833-818-ONCO(6626)</b>
<b>Kelowna</b>	<p>Between 9:00 am 4:00 pm Monday to Friday (excluding Statutory holidays) call:</p> <ul style="list-style-type: none"> <li>• Telephone Nurse Line call <b>(250) 712-3944</b> or</li> <li>• <b>1-888-563-7773 ext. 683944</b></li> </ul> <p>Outside these hours, call the Kelowna General Hospital switchboard at (250) 862-4000 and ask for the on-call medical oncologist.</p>

<b>BC CANCER CENTRES</b>	<b>FOR HEALTHCARE PROVIDERS:</b> <i><b>*To contact a patient's medical oncologist/hematologist directly by calling the centre's switchboard as listed below.</b></i>
<b>Abbotsford</b>	Call the Abbotsford Regional Hospital and Cancer Centre switchboard at (604) 851-4700 and ask for the patient's oncologist/hematologist, or after hours, for the on-call medical oncologist.
<b>Kelowna</b>	Call the Kelowna General Hospital switchboard at (250) 862-4000 and ask for the on-call medical oncologist.
<b>Prince George</b>	Call University Hospital of Northern British Columbia switchboard at (250) 565-2000 and ask for the on-call medical oncologist.
<b>Surrey</b>	Call the Surrey Memorial Hospital switchboard at (604) 581-2211 and ask for the Surrey on-call medical oncologist.
<b>Vancouver</b>	Call the BC Cancer Switchboard at (604) 877-6000 and press 1 and ask for the on-call medical oncologist.
<b>Victoria</b>	Call the Royal Jubilee Hospital switchboard at (250) 370-8000 and ask for the on-call medical oncologist.