

To: Emergency Department Physician/Nurse

RE: CHECKPOINT INHIBITOR AND CHEMOTHERAPY ADVERSE REACTION

From: Dr. _____ (patient's oncologist or hematologist) at
_____ (cancer centre)

This patient has received treatment with **Checkpoint Inhibitor (CPI) and Chemotherapy** called:

CPI can cause **immune-related side effects** because of unintended tissue injury after treatment, and any organ system may be involved. These side effects may be severe or life-threatening, and need different management from chemotherapy associated toxicities. If you suspect immune-related side effects, contact the oncologist listed above (or covering designate). With prompt management, these side effects are generally reversible, however immunosuppression may be needed.

Signs and symptoms suggestive of immune-related side-effects:	
Gastrointestinal: ♦ Colitis ♦ Pancreatitis ♦ Enteritis ♦ Hepatitis	<ul style="list-style-type: none"> • Diarrhea • Nausea • Elevated lipase • Gastrointestinal bleeding • Elevated liver enzymes • Abdominal pain/cramping
Pulmonary: ♦ Pneumonitis	<ul style="list-style-type: none"> • Shortness of breath • Chest pain • Cough • Fever
Skin: ♦ Dermatitis	<ul style="list-style-type: none"> • Pruritic rash
Endocrine: ♦ Hypophysitis ♦ Adrenal failure ♦ Thyroiditis ♦ Hypothyroidism ♦ Diabetes	<ul style="list-style-type: none"> • Fatigue, lethargy • Dehydration • Hypotension • Headache, visual disturbances • Mental status changes
Musculoskeletal: ♦ Arthritis ♦ Myositis	<ul style="list-style-type: none"> • Joint pain/swelling • Fatigue/myalgias
Neurological: ♦ Peripheral neuropathy ♦ CNS inflammation	<ul style="list-style-type: none"> • Numbness/pain • Mental status change • Headache • Focal neurological deficit
Renal: ♦ Acute kidney injury	<ul style="list-style-type: none"> • Swelling • Elevated serum creatinine
Cardiac: ♦ Myocarditis ♦ Pericarditis	<ul style="list-style-type: none"> • Chest pain • Fever • ECG changes • Elevated cardiac enzymes

Chemotherapy - This patient has been told to report to the ER as soon as possible if febrile (a single oral temperature of 38.3°C/100.9°F or higher or of 38.0°C/100.4°F measured at two occasions, one hour apart). Left untreated, it could lead to life-threatening sepsis. If febrile, they should have a history and physical exam to determine the site of infection, chest X-ray and a complete hematological and chemistry profile (see table below)

Recommendation	Notes
CBC with differential/absolute neutrophil count (ANC)	Neutropenia is an absolute neutrophil count (ANC) less than 0.5x10 ⁹ cells/L or an ANC less than 1.0x10 ⁹ cells/L with an expected fall to less than 0.5x10 ⁹ cells/L within the next 48 hours
Blood cultures x 2	
Electrolyte panel	
CR, Bilirubin, Alk Phos, Transaminases (ALT or AST)	
Urinalysis and culture	Absence of pus cells on urinalysis does not rule out UTI in the setting of neutropenia
Sputum gram stain and culture	If productive
Nasopharyngeal swab for viral respiratory panel PCR	If respiratory symptoms are present

Treatment - No focus of infection identified and **ANC is between 0.5 and 1.0x10⁹ cells.**

Call the oncologist/hematologist for antibiotic administration, hospitalization or follow-up arrangements

Treatment Recommendations – Focus of infection identified or ANC is less than 0.5x10⁹ cells	
Combination therapy	<ul style="list-style-type: none"> Piperacillin-tazobactam 4.5 grams IV every 8 hours Hemodynamically unstable or septic shock patients: β-Lactam plus an aminoglycoside plus vancomycin until C&S results are available [Vancomycin 15 mg per kg IV every 12 hours, with either gentamicin 5-7 mg/kg IV every 24 hours or tobramycin 7 mg/kg IV every 24 hours].
Monotherapy (alternative for patients allergic to penicillin)	<ul style="list-style-type: none"> Cefepime 2 grams IV every 8 hours for penicillin-allergic or anaphylactic patients. Alternatives include combination therapy listed above, Carbapenem monotherapy or empiric vancomycin listed below. Carbapenem monotherapy. In order to prevent carbapenem resistance, carbapenems should not be used in first line unless there is a known or suspected infection with ESBL/Amp C cephalosporinase-producing organisms or a penicillin allergy.
Empiric vancomycin	Consult guideline www.ahs.ca/guru (Symptom Management > Febrile Neutropenia)

Daytime Weekdays	
Calgary	403-521-3735 or 1-844-465-6330. After hours, weekends and holidays call the Foothills Medical Centre at 403-944-1110 (ask for oncologist/hematologist on call)
Edmonton	780-432-8771 or 1-877-707-4848. After hours, weekends and holidays call 780-432-8771 (ask for medical oncologist on call)
Grande Prairie 780-538-7588	Lethbridge 403-388-6800
Medicine Hat 403-529-8817	Red Deer 403-343-4526
After Hours	
RAAPID North at 1-800-282-9911	RAAPID South at 1-800-661-1700