Antineoplastic Chemotherapy Infusion Reactions: Hypersensitivity/Allergic

Site Applicability

PHC Sites where antineoplastic chemotherapy medications are administered

Practice Level

Basic Skill: Registered nurses

Need to Know

Preprinted prescriber's orders for hypersensitivity reaction should be completed whenever hypersensitivity high-risk medications are ordered.

There are 3 different kinds of reactions that a person may experience as a result of cancer chemotherapy drug treatment:

1. Allergic Reactions
   - Hypersensitivity
   - Anaphylaxis
2. Cytokine Release Reactions
3. Tumor Lysis Syndrome

The three kinds of reactions are discussed in separate practice standards – this standard discusses hypersensitivity/anaphylactic reactions.

Hypersensitivity Reactions and Anaphylaxis

Hypersensitivity and anaphylaxis are mediated by the immune system and are allergic in nature. The allergen may be a chemotherapy or biotherapy drug, its metabolites, or the drug diluent. The agents cause mast cell and basophil degranulation resulting in the release of mediators such as histamine. Symptoms suggestive of anaphylaxis are a result of the released mediators.

Anaphylaxis

Anaphylaxis is a distinct reaction that is rare with most conventional cytotoxic agents, although it is well established with the platinum drugs.

Anaphylaxis is a systemic event and is characterized by involvement of one or more body systems in addition to the skin (most anaphylactic reactions involve the skin). Urticaria (hives) and angioedema (swelling underneath the skin) are the most common manifestations of anaphylaxis and often occur as

the initial signs of severe anaphylaxis. The neck, trunk, abdomen, and axilla are sites where urticaria usually first appears.

Patients with even mild symptoms of mast cell/basophil activation (i.e. urticaria and dyspnea) must be treated with caution, because re-exposure to the causative agent could result in a fulminant and severe anaphylaxis.

Protocol

Assessment

To help determine the degree of intervention required, infusion reactions are broken down into those reactions considered mild, and those that are considered severe.

Mild reactions present with:

- Mild flushing
- Mild rash; itching

Severe reactions present with:

Acute onset of an illness (minutes to several hours): Cutaneous symptoms – flushing, pruritus, urticaria (hives)*, angioedema* AND AT LEAST ONE OF:

- Respiratory symptoms – dyspnea, wheeze, stridor, hypoxemia, sudden nasal congestion, repetitive cough, change in voice quality
- Hypotension or associated symptoms – collapse, syncope, incontinence

***** OR *****

2 OR MORE of the following occur rapidly after exposure to a likely allergen:

- Cutaneous symptoms
- Respiratory symptoms
- Hypotension or associated symptoms
- Gastrointestinal symptoms – nausea, vomiting, diarrhea, abdominal cramping
- Uterine cramping

***** OR *****

Hypotension after exposure to a known allergen for that patient:

- Systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline (taken immediately before start of chemotherapy administration)

Keep in mind:

- Skin symptoms and signs are present in up to 90 percent of anaphylactic episodes
- Mild reactions can progress to severe reactions rapidly

(also see Appendix B)

Risk Factors for Hypersensitivity Reactions

An increased risk of hypersensitivity reaction is known to occur with:

- Chemotherapy drugs and biologic agents. Those commonly associated with hypersensitivity reactions include:
  - **asparaginase** – risk is 5% to 8% per administered dose and increases with the number of doses. By the 4th dose up to 33% of patients experience a reaction. Skin testing to determine sensitivity is often done before the first dose is administered.
  - **bleomycin** – incidence is approximately 1%
  - **etoposide** & **teniposide** – 6% to 41% risk of hypersensitivity reaction and an anaphylaxis incidence of 0.7% to 14%
- IV route of administration
- Higher dosages
- Short intervals between exposures
- History of prior anaphylaxis (to foods, antibiotics, insect bites, radio-contrast media)
- History of allergies
- Female gender

Preparedness

1. **Equipment**

   All care settings where patients receive chemotherapy drugs should ensure that there is easy and ready to use access to:

   - oxygen
   - ambu-bag (resuscitation bag-valve-mask)
   - suction
   - IV access, supplies, and fluids

2. **Medications** (Physicians order required see PHC-PH581)

   A combination of medications is often necessary to manage a hypersensitivity reaction. First-line medications used in the management of a hypersensitivity reaction include:

   - EPInephrine for injection
   - diphenhydrAMINE for injection
   - hydrocortisone for injection
   - salBUTamol (VENTOLIN) and ipratropium (ATROVENT) for inhalation (by nebulization)

3. Patient Health History

Prior to the initiation of treatment with any chemotherapy or biotherapy drug:

- Obtain a detailed history of allergies and reactions to previous drug treatment – *a previous history of hypersensitivity reactions, even to structurally unrelated drugs, increases the patient's risk of subsequent reactions*.
- Ensure that the caution sheet is updated, completed, and faxed
- Complete a thorough baseline assessment including:
    - vital signs
    - oxygen saturation
    - breath sounds
    - presence of any rashes

4. Prophylaxis

Pharmacological prophylaxis with antihistamines and corticosteroids is generally recommended to reduce the frequency and severity of hypersensitivity reactions, particularly for drugs that have a high risk of reaction or for patients with a history of hypersensitivity reactions. Medications commonly used include:

- dexamethasone 20 mg PO 6 hours before initiation of chemotherapy and again 12 hours after chemotherapy
- diphenydrAMINE 50 mg IV 30 minutes before initiation of chemotherapy
- acetaminophen 650 mg PO 30 minutes before initiation of chemotherapy

Interventions

Monitoring

Patients should be monitored with constant visual observation during initiation, at all dose increases and for 30 minutes after infusion is completed.

Treatment and Management

In the event of **ALL suspected mild or severe hypersensitivity reactions**:

- Remove all suspected allergens. If receiving IV medication, stop medication and change IV tubing
- Sodium chloride 0.9% IV 100 mL/hour
- Notify physician
- Monitor vital signs Q5 minutes until stable
- Resume infusion as per physician's orders

If you suspect that your patient is having a **mild** hypersensitivity reaction (**mild** flushing; **mild** rash and itching):

- Administer diphenhydrAMINE 25 to 50 mg IV push or IM if IV access no longer available

If you suspect that your patient is experiencing a **severe** hypersensitivity reaction = cutaneous symptoms **and any one of**: respiratory compromise, GI symptoms, uterine cramping, or hypotension:

- Call Code Blue
- Administer:
  - EPInephrine 1:1000 (1 mg/mL) 0.5 mL IM into thigh STAT. Repeat Q5 minutes if symptoms persist or worsen. May administer a maximum of 3 doses. EPInephrine is the first-line treatment for severe hypersensitivity/anaphylactic reactions – delay in treatment is associated with increased mortality; administer as soon as systemic symptoms are detected/observed – there are no contraindications to EPInephrine.
  - diphenhydrAMINE 50 mg IV direct (or IM if no IV access available into a different site than that of the EPInephrine) x 1 dose if not already administered
  - If respiratory symptoms:
    - salBUTamol 5 mg via nebulizer Q20 minutes PRN x 3 doses
    - ipratropium bromide 0.5 mg via nebulizer Q20 minutes x 3 doses PRN severe bronchospasm
  - hydrocortisone sodium succinate 100 mg IV push x 1 dose

Documentation

1. Nursing documentation as per unit procedure: record assessment, nursing interventions, patient's response and vital signs
2. Medication Administration Record—any medications given

Patient and Family Education

Patients must be informed of potential side effects of the drugs, including the risk of a hypersensitivity reaction and the associated symptoms. It is essential that patients understand the importance of reporting any unusual symptoms. Patients and/or family members should be advised to notify a clinician immediately if they notice any discomfort during the infusion. Clinicians should observe patients for:

- restlessness
- fidgeting
- scratching
- clearing throat
- change in mood
- frequent changes in position

Any of the above may indicate that the patient is experiencing a hypersensitivity reaction.

Provide emotional support to the patient and their family – a hypersensitivity reaction is a very frightening experience.

Remain with the patient and family if you can – ensure that their questions have been answered and that their concerns have been addressed.

Related Documents

1. Chemotherapy: Infusion Reactions – Cytokine Release Syndrome (development)
2. Chemotherapy: Infusion Reactions – Tumor Lysis Syndrome (Development)
3. NCS6441 – Administration of Parenteral Antineoplastic Drugs (Hematology)
4. BD-00-12-40091 - Anaphylaxis: Initial Emergency Treatment
5. PHC-PH581 –Chemotherapy Hypersensitivity Pre-Printed Orders

References

1 BC Cancer Agency (2011). BCCA Protocol Summary for Management of Hypersensitivity Reactions to Chemotherapeutic Agents. Retrieved May 23, 2018 from http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Supportive%20Care/SCDRUGRX_Protocol_1Jan2011.pdf

2 Castells, M; Matulonis, UA; Horton, TM (2018). Infusion reactions to systemic chemotherapy. Retrieved May 23, 2018 from https://www.uptodate.com/contents/infusion-reactions-to-systemic-chemotherapy?search=hypersensitivity%20reaction%20chemotherapy&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

3 Castells, M (2015). Anaphylaxis to Chemotherapy and Monoclonal Antibodies. The Immunology and Allergy Clinics, 35

4 CRNBC (2018). Scope of Practice for Registered Nurses. Retrieved June 4, 2018 from https://www.crnbc.ca/Standards/Lists/StandardResources/433ScopeforRegisteredNurses.pdf

5 Lockey, RF. Anaphylaxis, Risk Assessment, and Use of Epinephrine. Retrieved May 23, 2018 from http://www.worldallergy.org/UserFiles/file/Treatment%20of%20Anaphylaxis-Lockey.pdf

6 Pichler, WJ (2018). Drug Allergy: Classification and clinical features. Retrieved May 23, 2018 from https://www.uptodate.com/contents/drug-allergy-classification-and-clinical-features?search=hypersensitivity%20reaction&sectionRank=1&usage_type=default&anchor=H31&source=machineLearning&selectedTitle=1~150&display_rank=1#H31

7 Simon, FER; Ebisawa, M; Sanchez-Borges, M; Thong, BY; Worm, M; Tanno, LK; Lockey, RF; El-Gamal, YM; Brown, SGA, Park, HS & Sheikh, A (2015). 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organization Journal, (8)80

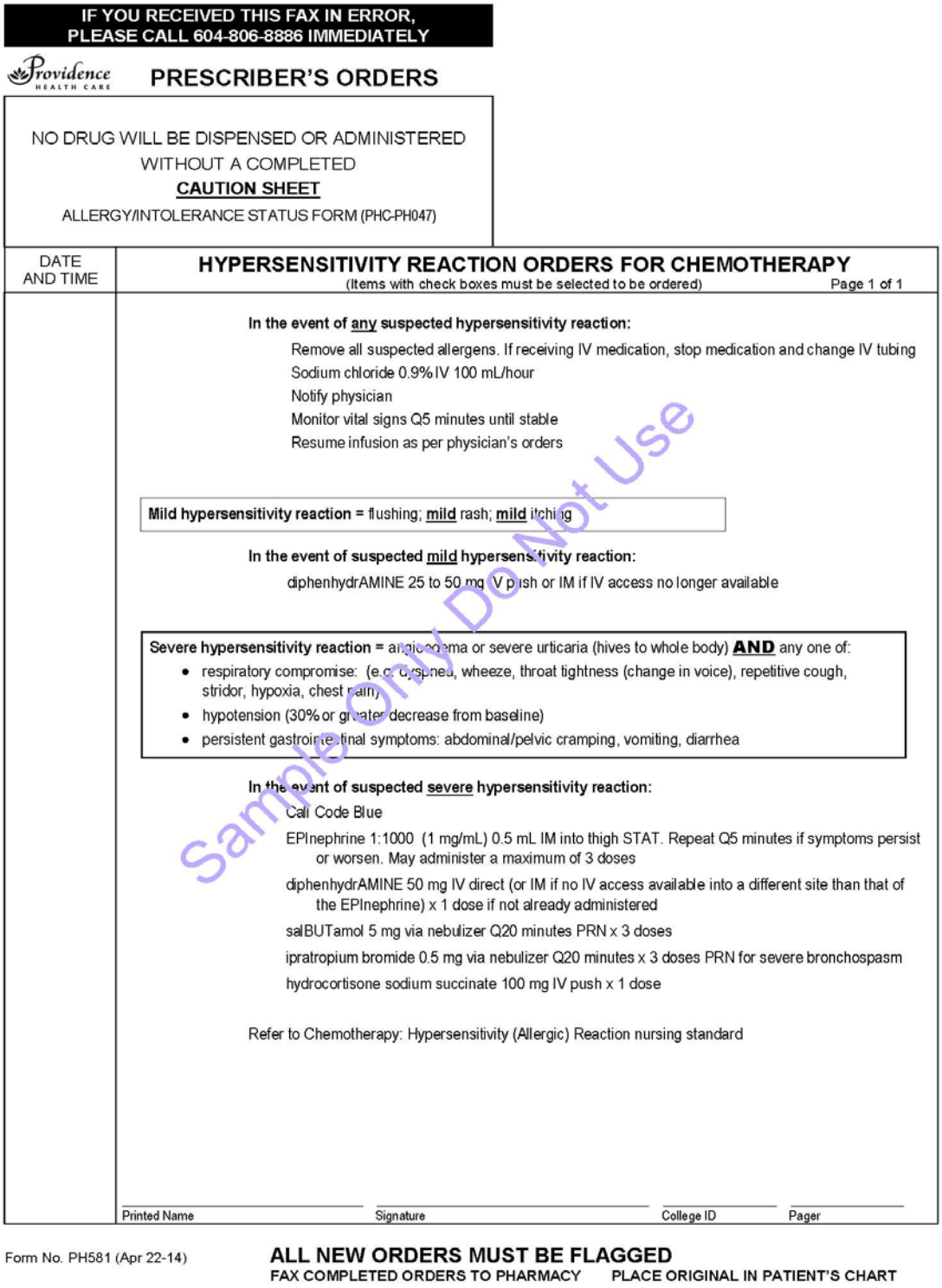
Persons/Groups Consulted:

TPN and Chemotherapy Pharmacist

Nurse Educators, Medicine

Author(s): Clinical Nurse Specialist Chemotherapy

Appendix A



IF YOU RECEIVED THIS FAX IN ERROR,
PLEASE CALL 604-806-8886 IMMEDIATELY

Providence HEALTH CARE

PRESCRIBER'S ORDERS

NO DRUG WILL BE DISPENSED OR ADMINISTERED
WITHOUT A COMPLETED
CAUTION SHEET
ALLERGY/INTOLERANCE STATUS FORM (PHC-PH047)

DATE AND TIME

HYPERSENSITIVITY REACTION ORDERS FOR CHEMOTHERAPY
(Items with check boxes must be selected to be ordered) Page 1 of 1

In the event of any suspected hypersensitivity reaction:

Remove all suspected allergens. If receiving IV medication, stop medication and change IV tubing
Sodium chloride 0.9% IV 100 mL/hour
Notify physician
Monitor vital signs Q5 minutes until stable
Resume infusion as per physician's orders

Mild hypersensitivity reaction = flushing; **mild** rash; **mild** itching

In the event of suspected mild hypersensitivity reaction:

diphenhydrAMINE 25 to 50 mg IV push or IM if IV access no longer available

Severe hypersensitivity reaction = angioedema or severe urticaria (hives to whole body) **AND** any one of:

- respiratory compromise: (e.g. dyspnea, wheeze, throat tightness (change in voice), repetitive cough, stridor, hypoxia, chest pain)
- hypotension (30% or greater decrease from baseline)
- persistent gastrointestinal symptoms: abdominal/pelvic cramping, vomiting, diarrhea

In the event of suspected severe hypersensitivity reaction:

Call Code Blue
EPInephrine 1:1000 (1 mg/mL) 0.5 mL IM into thigh STAT. Repeat Q5 minutes if symptoms persist or worsen. May administer a maximum of 3 doses
diphenhydrAMINE 50 mg IV direct (or IM if no IV access available into a different site than that of the EPInephrine) x 1 dose if not already administered
salBUTamol 5 mg via nebulizer Q20 minutes PRN x 3 doses
ipratropium bromide 0.5 mg via nebulizer Q20 minutes x 3 doses PRN for severe bronchospasm
hydrocortisone sodium succinate 100 mg IV push x 1 dose

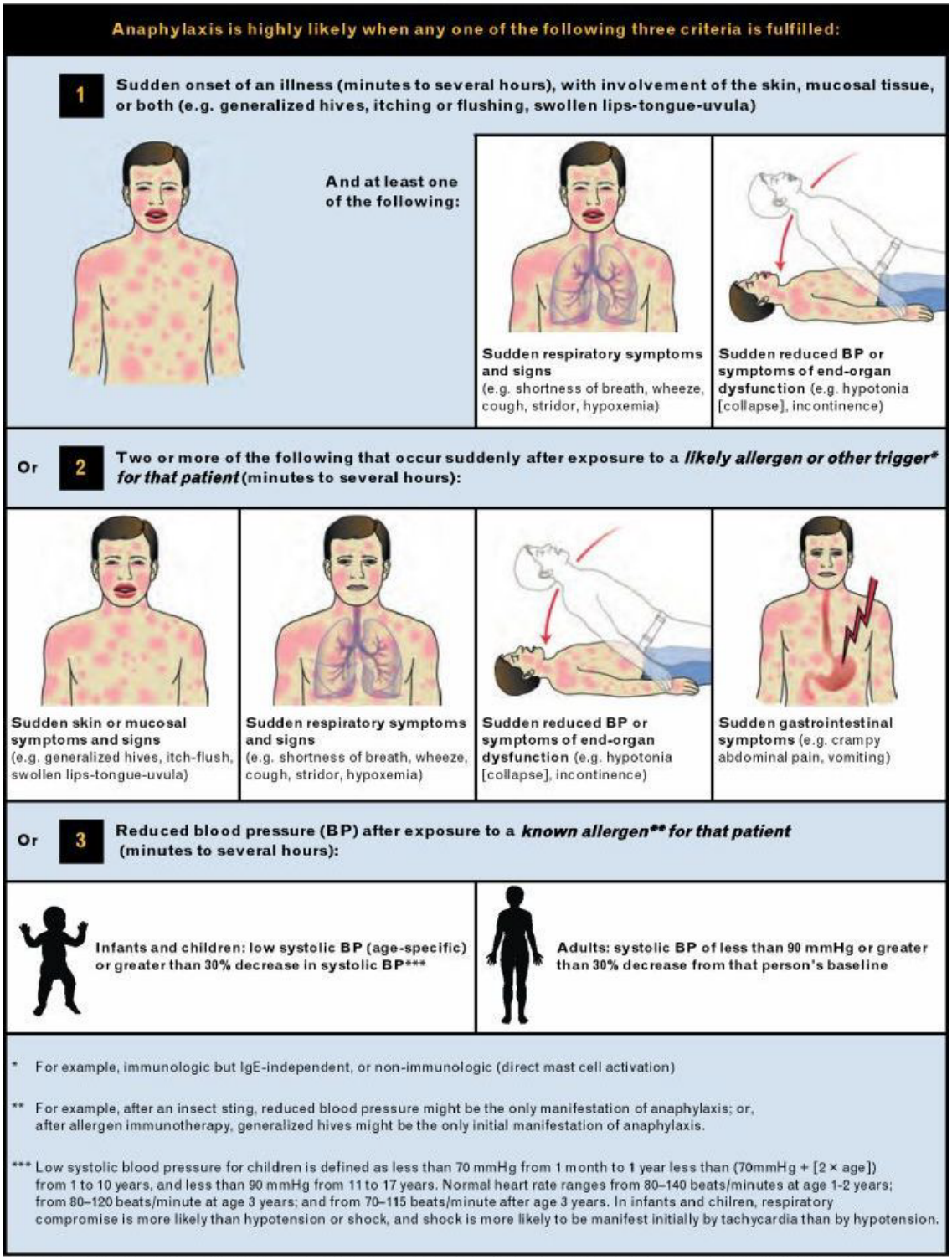
Refer to Chemotherapy: Hypersensitivity (Allergic) Reaction nursing standard

Printed Name | Signature | College ID | Pager

Form No. PH581 (Apr 22-14)

ALL NEW ORDERS MUST BE FLAGGED
FAX COMPLETED ORDERS TO PHARMACY PLACE ORIGINAL IN PATIENT'S CHART

Appendix B



From Simons FE, et al. World Allergy Organization guidelines for the assessment and management of anaphylaxis. World Allergy Organization Journal. 2011, 4:13-37.

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