

**Manitoba Interim Guidance for Immunocompromised  
Individuals Presenting with Symptoms of Acute Respiratory Illness During a  
Pandemic Influenza Period (H1N1)**

[http://www.gov.mb.ca/health/publichealth/sri/docs/immunocomp\\_respiratory\\_guidelines.pdf](http://www.gov.mb.ca/health/publichealth/sri/docs/immunocomp_respiratory_guidelines.pdf)

This document has been developed to provide interim guidance to clinicians for immunocompromised patients (please see definition below) presenting with influenza-like illness (ILI). This guideline should be used in conjunction with the following other Manitoba Health and Healthy Living guidelines all available at:

<http://www.gov.mb.ca/health/publichealth/sri/index.html> .

- *Manitoba Interim Guidance for Clinicians in Ambulatory Care Settings for Adults and Adolescents Presenting with Symptoms of Acute Respiratory Illness During a Pandemic Influenza Period (H1N1)*
- *Clinical Decision Making Algorithm for **Adults/Adolescents** Presenting with Symptoms of Acute Respiratory Illness During a Pandemic Influenza Period (H1N1)*
- *Pediatric Clinical Decision Making Algorithm Presenting with Symptoms of Acute Respiratory Illness During a Pandemic Influenza Period (H1N1)*
- *Manitoba Interim Clinical Care Guidance for Pregnant and Post-partum Women Presenting with Symptoms of Acute Respiratory Illness During a Pandemic Influenza Period (H1N1)*

**DEFINITIONS**

**Persons who may be Immunocompromised**

An immunocompromised patient may be recognized by having any single criterion from the following lists of Clinical Circumstances, Treatment Regimens or Laboratory Findings.

**Clinical Circumstances:**

The clinical circumstances associated with an immunosuppressed and/or myelosuppressed state include active treatments or disease entities. Such clinical circumstances may include but are not limited to the following:

- persons with malignancies receiving active cytotoxic chemotherapy,
- acute leukemia patients or those with lymphoreticular malignancies,
- hematopoietic stem cell transplant (HSCT) recipients,
- Solid organ transplant (SOT) recipients (e.g., lung, heart, kidney)
- Congenital and/or acquired immunodeficiency states (e.g., severe combined immunodeficiency and Human Immunodeficiency Virus infection, respectively.
- persons on kidney dialysis,
- persons with asthma or COPD
- Other autoimmune diseases treated with immunosuppressive medications including but not limited to diseases of the musculoskeletal, gastrointestinal, neurological, renal and dermatological systems.

**OR**

**Treatment Regimens:**

A history of ongoing administration of myelosuppressive and/or immunosuppressive treatments such as:

- corticosteroids (i.e.,  $\geq 1$  mg/kg/day OR  $\geq 10$  mg/day for  $\geq 4$  weeks OR  $\geq 20$  mg/day for  $\geq 2$  weeks)
- cytotoxic therapy (e.g., anthracyclines such as doxorubicin or epirubicin; purine analogues such as azathioprine, thioguanine, mercaptopurine, fludarabine, pentostatin, or cladribine; pyrimidine analogues such as fluorouracil, cytarabine, capecitabine, or gemcitabine; anti-folate agents such as methotrexate or pemetrexed; alkylating agents such as the nitrogen mustards (cyclophosphamide or ifosfamide), nitrosoureas (carmustine, lomustine, semustine, streptozotocin), and platinum analogues (cis-platin, carboplatin, or oxaliplatin); taxanes such as docetaxel or paclitaxel; topoisomerase I inhibitors such as irinotecan),
- immunomodulator therapies:
  - Calcineurin inhibitors (e.g., cyclosporine, tacrolimus, sirolimus),
  - Guanine synthesis inhibitors (e.g., Mycophenolate mofetil),
  - anti-B lymphocyte therapy (e.g., rituximab),
  - anti-T lymphocyte therapy (e.g., anti-thymocyte globulin or anti-CD3),
  - anti- B and T cell therapy (e.g., alemtuzumab, basiliximab, daclizumab),
  - anti-TNF therapy (e.g., infliximab, adalimumab or etanercept),
- alpha-interferon therapy

OR

**Laboratory Findings:**

- Severe neutropenia (i.e., absolute neutrophil count [ANC] of  $< 0.5 \times 10^9/L$ ) lasting longer than 7 days which may or may not be accompanied by lymphopenia;
- or
- Severe lymphopenia (i.e., ALC  $< 0.5 \times 10^9/L$ ) lasting longer than 7 days which may or may not be accompanied by severe neutropenia;
- or
- CD4 count  $< 200$  cells/mm<sup>3</sup> in an HIV positive individual

**Severely Immunocompromised Persons**

Severe immunocompromise may be said to be present when one of the "Laboratory Findings" above is present with any of the Clinical Circumstances or Treatment Regimens defined above.

**INFECTION PREVENTION AND CONTROL (IPC)**

For additional management details, this document should be used in conjunction with Manitoba Health and Healthy Living's *Infection Prevention and Control Guidelines Influenza-like illness including NOVEL A/H1N1 Influenza: All Health and Health-Care Settings* and additional infection prevention and control documents available at: <http://www.gov.mb.ca/health/publichealth/sri/index.html> . Clinicians should also refer patients to measures for reducing the risk of transmission of influenza and other respiratory illnesses in the home and in the community such as hand hygiene and cough etiquette available at: <http://www.gov.mb.ca/flu/factsheets.html>

**Entry screening in ambulatory health care settings for patients with symptoms of an acute respiratory illness:**

Refer to Manitoba Health and Healthy Living's *Acute Care Settings-Summary of Infection Prevention and Control Guidelines* available at: <http://www.gov.mb.ca/health/publichealth/sri/docs/acs.pdf> . All patients who present to a

health care setting should be screened for history of fever and respiratory symptoms. This could include:

- visual alerts posted at the entrances to all health care institutions and/or
- On first contact, receptionist staff should ask about fever and cough as well as other respiratory symptoms (sneezing, sore throat, coryza or runny nose). Patients with shortness of breath or severe weakness should be triaged for immediate care.

If transfer to hospital is required, routine infection control practices, including droplet and contact precautions, should be followed.

**Patients who report fever and respiratory symptoms should be instructed to:**

- Clean their hands with 60-90% alcohol-based hand gel
- Don a surgical or procedure mask
- Be separated by at least one metre from others, and if feasible, a two metre separation may be preferred. Infection Prevention and Control signage should be placed on the door indicating precautions required.

**Additional Considerations for Immunocompromised Patients:**

- Hospital infection prevention and control procedures should be followed for persons in hospital settings.
- Viral shedding in immunocompromised patients may be significantly longer (weeks to months versus days) and associated with a higher risk for communicability in the community and hospital setting. Therefore these persons should continue good hand hygiene and respiratory hygiene practices during the entire period on therapy and while still symptomatic to prevent the transmission of virus to close contacts (3). Infection Prevention and Control should be consulted for duration of isolation precautions while in hospital.

**CASE DEFINITIONS AND CLINICAL PRESENTATION**

**Symptoms of Mild Influenza Like Illness (ILI)**

For the purposes of guiding healthcare providers, the following Public Health Agency of Canada (PHAC) influenza-like illness surveillance case definition remains the basis for consideration of the presence of any influenza type, including pandemic H1N1:

Acute onset of respiratory illness with fever and cough and one or more of the following:  
sore throat, arthralgia, myalgia or prostration.

**Note I:** Not all cases of severe pandemic H1N1 have presented with symptoms consistent with the above definition. The following symptoms have been observed during the first wave of pandemic H1N1 and should also be considered in the clinical diagnosis of ILI at this time.

Almost always:

- **Cough and Fever**

Common:

- **Fatigue, muscle aches, sore throat, headache**

Sometimes:

- **Nausea, vomiting, diarrhea**

**Note II:**

- Immunocompromised persons may not present with typical signs and symptoms of ILI, as they may be muted due to treatment or disease related suppression of the normal inflammatory response.
- High fevers and myalgias may be less prominent compared with healthy individuals.
- Oncology patients are more likely to have a “mild” illness initially that may progress to pneumonia, and with that a greater chance of life-threatening illness.
- The signs and symptoms of ILI, particularly fever, may be muted in very young patients.

**Warning signs and symptoms indicative of pending serious illness that warrant admission to hospital for observation for at least 24 hours, with appropriate medical and transportation provisions for intensive care admission if needed:**

- Tachypnea RR > 30
- Dyspnea or shortness of breath
- Cyanosis
- Hypoxemia (SaO<sub>2</sub> < 92%)
- Purulent or bloodstained sputum
- Chest pain or pleuritic chest pain
- Persistent tachycardia HR > 100
- Dehydration and hypotension
- Rigors
- Altered mental status
- Persistent fever beyond 3 days, despite therapy

## **REPORTING RESPONSIBILITIES**

Clinicians are required to report within 24 hours any current or recent case(s) of ILI resulting in hospitalization. The “Hospitalized Influenza-Like Illness (ILI) Reporting Form” (available at: <http://www.gov.mb.ca/health/publichealth/sri/index.html#forms> ) can be faxed to the Surveillance Unit, Public Health Division, Manitoba Health and Healthy Living at (204) 948-3044 or a verbal report can be made by leaving a message at (204) 788-6481 or other arrangements can be made as approved by the Regional Medical Officer of Health.

The previous case report form titled “Severe Respiratory Illness/Novel Influenza A H1N1 Case Report Form” has been revised and renamed the “Pandemic H1N1/Severe Respiratory Case Report Form (available at: <http://www.gov.mb.ca/health/publichealth/sri/index.html#forms>). This form should be completed for all patients admitted to hospital and diagnosed with either pandemic H1N1 or SRI or for any patient who dies in hospital and the death is suspected to be H1N1 or SRI related. Completed forms should be faxed to the Surveillance Unit, Public Health Division, Manitoba Health and Healthy Living at (204) 948-3044.

## **VIRAL TESTING**

Recommendations for nasopharyngeal (NP) swabbing/sampling and policies for laboratory testing may change as the pandemic H1N1 outbreak progresses, and may vary depending upon prevalence, relative presence of antiviral resistance, laboratory and other resources, and other factors. The following guidelines refer to recommendations for obtaining test specimens in the clinical setting. Because clinical decision-making for non-severe cases should rarely, if ever, depend on the results of a test for influenza, laboratory testing will be performed on a priority basis and not necessarily on every specimen submitted, considering the information available on the requisition and other factors, including those described above.

**Please note that testing is not required in order for treatment to be initiated.**

**Cadham Provincial Laboratory (CPL) will not process specimens for pandemic H1N1 testing unless one or more of the following indications are present on the CPL requisition for clients/patients with ILI:**

- a. hospitalized patients (for differential diagnosis and monitoring for severity);
- b. immunocompromised patients (monitoring for antiviral resistance);
- c. patients being observed in emergency departments, observation units, etc (for surveillance);
- d. patients seen at designated sentinel sites, as authorized by regional and provincial public health authorities (for surveillance).

If the indication and other information are not recorded, specimen testing may be delayed. In exceptional circumstances, specimens may not be tested. Inadequately labeled and packaged specimens (e.g., leaking) may not be processed. For outbreak investigation, testing should only be performed in consultation with a public health professional. The laboratory will communicate positive test results for pandemic H1N1 influenza to those ordering the testing on a priority basis, based on information provided on the requisition.

**If testing is indicated:**

- A well taken nasopharyngeal swab is preferred but an oropharyngeal swab, tracheal aspirate or bronchial wash may be appropriate in some circumstances.
- A nasopharyngeal aspirate should be taken for children < 5 years of age. For all others, a nasopharyngeal swab is preferred. Pediatric swabs, if available, are preferred for use in the 5 to 15 year population.
- Excess mucous should be removed before specimen collection. In all cases, the specimen should be collected with a nasopharyngeal (wire) swab or flocked (microRheologics) swab and placed in viral transport medium (VTM). Only one specimen per patient is required. A fact sheet about these procedures for testing can be found at: [http://www.gov.mb.ca/health/publichealth/sri/docs/nasopharyngeal\\_collection.pdf](http://www.gov.mb.ca/health/publichealth/sri/docs/nasopharyngeal_collection.pdf)
- Ensure the correct viral flocked swab and transport medium is used and that it is not past its expiry date.
- An appropriately labeled Cadham Provincial Laboratory requisition MUST accompany the specimen. Ensure that both the specimen and the requisition are clearly labeled with the specimen date, patient's name and another unique identifier such as date of birth and health care number. If urgent reporting of test results is requested by the clinician (rarely required for clinical decision-making), the requisition should include a practitioner telephone number or information for other faster methods of reporting. Requisitions without clinical information will be prioritized last. Important information includes:
  - Underlying medical conditions;
  - Date of onset of symptoms;
  - Symptoms and signs;
  - Hospitalized or not;
  - Prescription date and/or start date of antiviral medications.
- A number label should be removed from the requisition and attached to the specimen.

**IMMUNIZATION**

All persons at high risk of seasonal influenza-related complications or who are more likely to require hospitalization should receive the annual seasonal influenza vaccine. This includes persons with cancer, immunodeficiency or immunosuppression (due to underlying disease and/or therapy)(6). Refer to the current *Canadian Immunization Guide* for information on timing of vaccination with respect to receipt of immunosuppressive therapy.

Recommendations regarding immunization for pandemic H1N1 influenza can be found in the following documents:

- *Priority Groups in Manitoba* available at: <http://www.gov.mb.ca/health/publichealth/sri/docs/priority.pdf>

- *Interim Guidelines for Using the Pandemic H1N1 (pH1N1) Influenza Vaccine* available at:  
[http://www.gov.mb.ca/health/publichealth/sri/docs/interim\\_guidelines\\_h1n1vaccine.pdf](http://www.gov.mb.ca/health/publichealth/sri/docs/interim_guidelines_h1n1vaccine.pdf)

Immunization with pandemic H1N1 influenza vaccine is also recommended for household contacts and care providers of persons who are immunocompromised.

## CLINICAL MANAGEMENT

The following recommendations apply to patients presenting with mild ILI with or without prior antiviral treatment and with or without previous immunization with seasonal or pandemic H1N1 vaccine. Severely immunocompromised patients are at increased risk for developing complications secondary to community-acquired respiratory virus infection. Follow-up is recommended for all patients who become symptomatic, even for those previously provided with a prescription and who have initiated antiviral therapy. **Consultation with Infectious Diseases (204-787-2071) is recommended to inform decision-making on specific cases.**

**TABLE 1: Recommended Clinical Case Management** (adapted with permission from Dr. Eric Bow, CancerCare Manitoba draft guidelines)

Circumstance	Exposure	Recommendation
1. Asymptomatic oncology/immunocompromised patient (i.e., may or may not meet the criteria for severe immunocompromise)	No history of contact <sup>a</sup> with pandemic H1N1 influenza	1. No treatment required 2. NP testing for H1N1 is not indicated
2. Asymptomatic oncology /immuno compromised patient that does not meet the criteria for severe immunocompromise.	History of contact <sup>a</sup> with pandemic H1N1 influenza	1. Consider providing with prescription for neuraminidase inhibitor with instructions that it should only be filled if symptoms develop. Provide information on which symptoms would trigger this. 2. Alternatively request that patient call back if symptoms develop, so that prescription can be provided by phone. 3. NP testing for H1N1 is not indicated.

<sup>a</sup> Close contact is defined as having cared for or lived with a person who is a suspected or confirmed case of influenza, or having been in a setting where there was a high likelihood of contact with respiratory droplets and/or body fluids of such a person during their period of communicability. The period of communicability is generally up to 7 days from onset of symptoms in uncomplicated cases. This period may be longer (up to 10 days) in individuals with severe illness (<http://www.phac-aspc.gc.ca/alert-alerte/h1n1/hp-ps/psili-eng.php>). Examples of close contact include sharing eating or drinking utensils or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person or sitting across from a symptomatic patient in a waiting room or office (3).

<p>3. Asymptomatic oncology /immuno compromised patient that meets the criteria for severe immunocompromise.</p>	<p>History of contact<sup>a</sup> with pandemic H1N1</p>	<ol style="list-style-type: none"> <li>1. Consider providing with prescription for neuraminidase inhibitor with instructions that it should only be filled if symptoms develop. Provide information on which symptoms would trigger this.</li> <li>2. Consider neuraminidase inhibitor chemoprophylaxis with oseltamivir (75 mg orally OD x 10 days) or zanamivir (two 5-mg inhalations OD x 10 days). If utilized it is recommended that chemoprophylaxis be initiated as soon as possible within 48 hours of exposure. Early recognition of illness and treatment when indicated is preferred to chemoprophylaxis for vaccinated persons after a suspected exposure (Oct.21, 2009 CDC guidelines <a href="http://www.cdc.gov/h1n1flu/guidance_HIV.htm">http://www.cdc.gov/h1n1flu/guidance_HIV.htm</a> Note: Oseltamivir resistance appears to be rare at this time. However oseltamivir resistant 2009 H1N1 viruses have been identified typically among persons who develop illness while receiving oseltamivir for chemoprophylaxis or immunocompromised patients with influenza who are being treated. These findings underscore the importance of limited use of antivirals for chemoprophylaxis.(3)</li> <li>3. NP testing for H1N1 is not indicated.</li> </ol>
<p>4. Symptomatic oncology/immuno compromised patient who meets ILI case definition (i.e., may or may not meet the criteria for severe immunocompromise)</p> <p>OR</p> <p>Symptomatic oncology/immuno compromised patients who do not meet the ILI case definition but for whom the clinician has a high index of suspicion/concern regarding H1N1 infection (e.g., patient does not have a fever but clinician suspects H1N1 infection).</p>	<p>With or without history of contact<sup>a</sup> with pandemic H1N1 influenza</p>	<ol style="list-style-type: none"> <li>1. Neuraminidase inhibitor treatment should be initiated as soon as possible unless contraindicated, and should be accompanied by a clinical assessment, (see Table 2 for dosing) – Start treatment as soon as possible within 48 hours.</li> <li>2. NP testing for H1N1 is recommended, but do not wait for test results.</li> <li>3. Consider initiation of antimicrobial therapy based upon clinical history and assessment.</li> <li>4. Hospitalization is recommended if one or more of the warning signs outlined in the clinical presentation section of this guideline (page 3) are present.</li> <li>5. Additional laboratory and diagnostic recommendations <ul style="list-style-type: none"> <li>• Blood cultures (peripheral and central venous access sites)</li> <li>• Lower respiratory tract secretions (sputum) for bacterial culture</li> <li>• Serology for <i>Chlamydia pneumoniae</i> and <i>Mycoplasma pneumoniae</i> PCR or culture</li> <li>• Chest x-ray (PA and lateral) and sinus x-rays as appropriate for the clinical findings.</li> </ul> </li> </ol>

**Table 2. Antiviral treatment dosing<sup>b</sup> recommendations for Adults and Children** [Table based on IDSA guidelines for seasonal influenza, *CID* 2009; 48: 1003-1032: [www.idsociety.org/content.aspx?id=9202#flu](http://www.idsociety.org/content.aspx?id=9202#flu) ) and Public Health Agency of Canada Interim Guidance for emergency use of oseltamivir (Tamiflu®) in children under one year of age in the context of 2009 (H1N1) pandemic at <http://www.phac-aspc.gc.ca/alert-alerte/swine-porcine/guidance-orientation-07-20-eng.php> ].

Age Group	Weight	Drug	Dosing Schedule
Infants and children	≤ 15 kg	Oseltamivir (Tamiflu®)	2 mg/kg/dose orally twice daily x 5 days
Children < 13 years of age	>15-23 kg	Oseltamivir (Tamiflu®)	45 mg orally twice daily x 5 days
	>23-40 kg	Oseltamivir (Tamiflu®)	60 mg orally twice daily x 5 days
	> 40 kg	Oseltamivir (Tamiflu®)	75 mg orally twice daily x 5 days
Adults and children ≥ 13 years of age		Oseltamivir (Tamiflu®)	75 mg orally twice daily x 5 days
Adults and children ≥ 7 years of age		Zanamivir (Relenza®)	2 inhalations twice daily x 5 days

<sup>b</sup>Dosages may need to be modified based on the presence of renal disease or other co-morbidities. Refer to product monograph for details, and/or consult with an Infectious Diseases specialist, Nephrologist or Pharmacist. For potential medication errors with liquid Tamiflu®, please see: [http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2009/2009\\_158-eng.php](http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2009/2009_158-eng.php) for more information.

**Other considerations for the use of antivirals for treatment of H1N1 influenza:**

Recommendations for use of antiviral medications may change as data on antiviral effectiveness, clinical spectrum of illness, adverse events from antiviral use, or resistance among circulating viruses become available (3). While oseltamivir resistance appears to be rare at this time, oseltamivir-resistant 2009 H1N1 viruses have been identified, typically among persons who develop illness while receiving oseltamivir for chemoprophylaxis or immunocompromised patients with influenza who are being treated (3). For more information on H1N1 antiviral resistant strains, refer to *WHO Pandemic (H1N1) 2009 briefing note 12- Antiviral use and the risk of drug resistance*.

[http://www.who.int/csr/disease/swineflu/notes/h1n1\\_antiviral\\_use\\_20090925/en/index.html](http://www.who.int/csr/disease/swineflu/notes/h1n1_antiviral_use_20090925/en/index.html)

It is recommended that household contacts of individuals with significant risk factors (e.g., immunocompromised hosts) be counseled about early signs and symptoms of pandemic H1N1 and encouraged to seek early treatment if symptomatic.

More information on both these antiviral medications (oseltamivir and zanamivir) including reconstitution guidelines/instructions can be found in the Product Monograph. For recent Health Canada drug advisories please refer to: <http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/new-neuf-advisories-avis-eng.php> . Adverse reactions should be reported to the Marketed Health Products Directorate at Health Canada at: [http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/guide/2009-ar-ei\\_anti\\_guide-ldir/index-eng.php](http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/guide/2009-ar-ei_anti_guide-ldir/index-eng.php) . Otherwise, treatment is supportive, such as acetaminophen-containing medications to ease fever and myalgias.

**References**

1. Public Health Agency of Canada. Interim Guidance for Ambulatory Care of Influenza-Like Illness in the context of H1N1 influenza virus, modified July 16, 2009, available at: <http://www.phac-aspc.gc.ca/alert-alerte/swine-porcine/guidance-orientation-amb-07-16-eng.php>
2. Harper Scott A, Bradley John S, Englund Janet A *et al.* Seasonal Influenza in Adults and Children—Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America. *Clinical Infectious Diseases* 2009; 48: 1003-1032 available at: <http://www.idsociety.org/content.aspx?id=9202#flu>
3. U.S. Centers for Disease Control and Prevention. Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010, October 16, 2009 Available at: <http://www.cdc.gov/h1n1flu/recommendations.htm>

4. Manitoba Health and Healthy Living: Severe Respiratory Illness / Novel Influenza A / H1N1 Case Report Form: Preliminary Case Analysis. June 12, 2009
5. World Health Organization. *Pandemic (H1N1) 2009 briefing note 12*) Antiviral use and the risk of drug resistance. Available at:  
[http://www.who.int/csr/disease/swineflu/notes/h1n1\\_antiviral\\_use\\_20090925/en/index.html](http://www.who.int/csr/disease/swineflu/notes/h1n1_antiviral_use_20090925/en/index.html)
6. Public Health Agency of Canada. *Guidance on H1N1 Vaccine Sequencing* Available at:  
<http://www.phac-aspc.gc.ca/alert-alerte/h1n1/vacc/pdf/vacc-eng.pdf>.
7. National Advisory Committee on Immunization (NACI). Statement on Influenza Vaccination for the 2008-2009 Season. July 2008, Volume 34, page 10.