

Adapted from a CDC Health Advisory

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## Interim Recommendations for the Use of Influenza Antiviral Medications in the Setting of Oseltamivir Resistance among Circulating Influenza A (H1N1) Viruses, 2008-09 Influenza Season

Although influenza activity is low in Canada to date, preliminary data from a limited number of provinces indicate that the current circulating influenza A (H1N1) virus strains are resistant to the antiviral medication oseltamivir and the current circulating Influenza A (H3N2) are resistant to amantadine. Therefore, the recommendations are provided below for antiviral treatment and chemoprophylaxis of influenza during the 2008-09 influenza season. As of December 22, 2008 the few circulating influenza A strains recognized in Alberta have been Influenza A (H3N2)

The 2008-09 influenza vaccine is expected to be effective in preventing or reducing the severity of illness with currently circulating influenza viruses, including oseltamivir-resistant influenza A (H1N1) virus strains. Since influenza activity remains low and is expected to increase in the weeks and months to come, the influenza vaccination efforts should continue.

### **Background**

Influenza A viruses, including two subtypes (H1N1) and (H3N2), and influenza B viruses, currently circulate worldwide, but the prevalence of each can vary among communities and within a single community over the course of an influenza season. In Canada, three prescription antiviral medications (oseltamivir, zanamivir, and amantadine) are approved for treatment and chemoprophylaxis of influenza. Since January 2006, the neuraminidase inhibitors (oseltamivir, and zanamivir) have been the only recommended influenza antiviral drugs because of widespread resistance to the adamantanes among influenza A (H3N2) virus strains. The neuraminidase inhibitors have activity against influenza A and B viruses while the adamantanes have activity only against influenza A viruses. In 2007-08, a significant increase in the prevalence of oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide.

Influenza activity has been low thus far this season. As of December 13, 2008, a limited number of influenza viruses isolated in Canada have been available for antiviral resistance testing at the NML. Of the 8 H1N1 viruses tested to date, 100% were resistant to oseltamivir, and all were susceptible to zanamivir and amantadine. Preliminary data indicate that oseltamivir-resistant influenza A

(H1N1) viruses do not cause different or more severe symptoms compared to oseltamivir sensitive influenza A (H1N1) viruses. Influenza A (H3N2) and B viruses remain susceptible to oseltamivir. The proportion of influenza A (H1N1) viruses among all influenza A and B viruses that will circulate during the 2008-09 season cannot be predicted, and will likely vary over the course of the season and among communities. Oseltamivir-resistant influenza A (H1N1) viruses are antigenically similar to the influenza A (H1N1) virus strain represented in 2008-09 influenza vaccine, and it is recommended that influenza vaccination efforts continue as the primary method to prevent influenza.

Oseltamivir resistance among circulating influenza A (H1N1) virus strains presents challenges for the selection of antiviral medications for treatment and chemoprophylaxis of influenza, and provides additional reasons for clinicians to test patients for influenza virus infection and to consult surveillance data when evaluating persons with acute respiratory illnesses during influenza season. These interim guidelines provide options for treatment or chemoprophylaxis of influenza if oseltamivir-resistant H1N1 viruses are circulating widely in a community or if the prevalence of oseltamivir resistant H1N1 viruses is uncertain.

### **Interim Recommendations**

Persons providing medical care for patients with suspected influenza or persons who are candidates for chemoprophylaxis against influenza should consider the following guidance for assessing and treating patients during the 2008-09 influenza season.

1. Review available influenza virus surveillance data weekly during influenza season, to determine which types (A or B) and subtypes of influenza A virus (H3N2 or H1N1) are currently circulating at the Flu Watch site: <http://www.phac-aspc.gc.ca/fluwatch> . For some communities, surveillance data might not be available or timely enough to provide information useful to clinicians.
2. Depending on the current circulating influenza strains (or point of care or other timely testing, if available)
  - If influenza B is predominant either oseltamivir or zanamivir (no preference) if treatment is indicated.
  - If influenza A (H3N2) is the circulating influenza A virus oseltamivir or zanamivir would be the drugs of choice for treatment.
  - If influenza A (H1N1) is the circulating influenza strain amantadine would be the drug of choice.
  - If both influenza A strains are circulating, use of zanamivir should be considered if treatment is indicated and the patient is able to take and tolerate an inhaled product. Oseltamivir should be used alone only if recent local surveillance data indicate that circulating viruses are likely to be influenza A (H3N2) or influenza B viruses. A combination treatment with oseltamivir and amantadine is a

possible alternative, and for patients who cannot receive zanamivir, (e.g., patient is <7 years old, those with chronic underlying airway disease, or cannot use the zanamivir inhalation device), or zanamivir is unavailable.

3. Persons who are candidates for chemoprophylaxis (e.g., residents in an assisted living facility during an influenza outbreak, or persons who are at higher risk for influenza-related complications and have had recent household or other close contact with a person with laboratory confirmed influenza) should be provided with medications most likely to be effective against the influenza virus that is the cause of the outbreak, if known. Respiratory specimens from ill persons during institutional outbreaks should be obtained and sent for testing to determine the type and subtype of influenza A viruses associated with the outbreak and to guide antiviral therapy decisions. Persons whose need for chemoprophylaxis is due to potential exposure to a person with laboratory-confirmed influenza A (H3N2) or influenza B should receive oseltamivir or zanamivir (no preference). Zanamivir should be used when persons require chemoprophylaxis due to exposure to influenza A (H1N1) virus.
4. Enhanced surveillance for influenza antiviral resistance is ongoing at the NML. Clinicians should remain alert for additional changes in recommendations that might occur as the 2008--09 influenza season progresses. Oseltamivir resistant influenza A (H1N1) viruses are antigenically similar to the influenza A(H1N1) viruses represented in the vaccine, and vaccination should continue to be considered the primary prevention strategy regardless of oseltamivir sensitivity. Information on antiviral resistance will be updated in weekly surveillance reports (available at <http://www.phac-aspc.gc.ca/fluwatch> ).