

## Antiviral medications for influenza: Information for health care providers

Updated December 2016

### What are antiviral medications for influenza?

Antiviral medications are recommended to treat and prevent influenza. Amantadine is an older antiviral medication that is no longer used. Drugs currently used in Canada are oseltamivir (Tamiflu®) which is an oral medication, and zanamavir (Relenza®) which is an inhaled medication. Oseltamivir and zanamivir are neuraminidase inhibitors which work by blocking the exit of the influenza virus from respiratory cells and therefore prevent further replication of the virus. Because antiviral medications prevent further replication of the virus, when used for treatment, they should be taken as soon as possible, ideally within 48 hours of symptom onset.

### What are the recommendations for the use of influenza antiviral medications?

Influenza antiviral medications are recommended for:

- Treatment of moderate, progressive, severe or complicated influenza, such as individuals who are hospitalized with influenza-like illness;
- Treatment of those at high risk for complications of influenza, such as children less than 5 years of age, adults 65 years of age and over, and those with underlying medical conditions (see [Appendix A](#) for additional details);
- Treatment and prevention in influenza outbreaks in institutional settings (see [How are antiviral medications used in institutional influenza outbreaks?](#)).

When influenza is circulating, laboratory confirmation of influenza is not needed before initiating treatment, as waiting until influenza is confirmed will delay initiation of therapy. Although treatment is generally more beneficial if given early, it can still be considered in those at high risk for influenza complications, even if more than 48 hours has passed from symptom onset. Use of antiviral medication is also recommended, regardless of time from symptom onset, in individuals with moderate, progressive, severe or complicated influenza-like illness, such as individuals who are hospitalized with influenza-like illness.<sup>1</sup>

### How can practitioners determine if influenza is circulating?

From November to April, Public Health Ontario posts a weekly [Respiratory Pathogen Surveillance Bulletin](#) which provides information about the circulation of influenza and other respiratory pathogens in Ontario. This report is posted every other week during other times of the year. Some local public health units also produce their own surveillance reports.

## How are influenza antiviral medications used?

The following describes key features related to the use of influenza antiviral drugs.

	Oseltamivir	Zanamivir (5 mg per inhalation)
<b>Dosage for treatment</b>	75 mg twice daily for 5 days for adults; See <a href="#">AMMI guideline</a> for pediatric dosing <sup>a</sup> ; Dose adjustments may be needed if person is known to have renal impairment. See <a href="#">AMMI guidelines</a> <sup>b</sup>	2 inhalations twice daily (approximately 12 hours apart) for 5 days <sup>c</sup>
<b>Dosage for prevention</b>	75 mg daily for 10 days for adults <sup>d</sup> (or in an outbreak, until the outbreak is declared over); See <a href="#">AMMI guidelines</a> for pediatric dosing <sup>a</sup> ; Dose adjustments may be needed if person is known to have renal impairment. See <a href="#">AMMI guidelines</a> <sup>b</sup>	2 inhalations once daily for 10 days
<b>Age authorized for use</b>	1 year of age and over; Can be considered on a case-by-case basis for those younger than 1 year of age. <sup>a</sup>	7 years of age and over
<b>Side effects</b>	Nausea, vomiting. Taking it with food may increase tolerability. Post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events (self-injury or delirium; mainly reported among Japanese adolescents and adults). <sup>e</sup>  See <a href="#">product monograph</a> for additional details	Allergic reactions: oropharyngeal or facial edema. Adverse events: diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infections <sup>e</sup>  See <a href="#">product monograph</a> for additional details
<b>Contra-indications</b>	None. <sup>e</sup>  See <a href="#">product monograph</a> for additional details	Underlying respiratory condition such as chronic obstructive pulmonary disease or asthma <sup>e</sup>  See <a href="#">product monograph</a> for additional details
<b>Product monograph</b>	<a href="http://www.rochecanada.com/content/dam/roche_canada/en_CA/documents/Research/ClinicalTrialsForms/Products/ConsumerInformation/MonographsandPublicAdvisories/Tamiflu/Tamiflu_PM_E.pdf">http://www.rochecanada.com/content/dam/roche_canada/en_CA/documents/Research/ClinicalTrialsForms/Products/ConsumerInformation/MonographsandPublicAdvisories/Tamiflu/Tamiflu_PM_E.pdf</a>	<a href="http://ca.gsk.com/media/535135/relenza.pdf">http://ca.gsk.com/media/535135/relenza.pdf</a>

- See Table 4 of the AMMI Canada Guidelines for pediatric dosing <https://www.ammi.ca/Content/Guidelines/Flu%20%28published%20version%29%20FINAL.pdf>
- Checking creatinine clearance and dose adjustments are not required for those who are not known to have renal impairment. For those with known renal impairment, alternative dosing based on creatinine clearance is provided in Table 5 of the AMMI Guidelines <https://www.ammi.ca/Content/Guidelines/Flu%20%28published%20version%29%20FINAL.pdf>
- A second dose (10 mg, which is 2 inhalations) should be taken on the first day of treatment whenever possible, provided there is at least 2 hours between doses (based on the product monograph <http://ca.gsk.com/media/535135/relenza.pdf>)
- For exposure to avian influenza, 75 mg twice a day is recommended for prevention <http://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm>
- Source: CDC Influenza Antiviral Medications: Summary for Clinicians <http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>

## Is influenza antiviral resistance a concern?

There is very little resistance to oseltamivir or zanamivir among recently circulating strains of influenza. Influenza strains are regularly monitored for antiviral resistance with results provided in the [Ontario Respiratory Pathogen Bulletin](#).

## How are antiviral medications used in institutional influenza outbreaks?

When an influenza outbreak is declared in an institutional setting, antiviral medications are recommended for:

- treatment of residents/patients meeting the case definition, regardless of immunization status;
- prophylaxis of residents/patients who are not ill with influenza symptoms, regardless of immunization status;
- prophylaxis of unvaccinated staff members;
- prophylaxis of vaccinated staff members when there is a mismatch between the vaccine and circulating influenza strains, based on consultation with public health officials.<sup>2</sup>

Antiviral medication for treatment and prophylaxis should begin as soon as possible in an outbreak. For prevention, the antiviral drugs should be used for the duration of the outbreak. For influenza outbreaks in long-term care homes, oseltamivir is the preferred antiviral for residents. Information on prophylaxis following treatment can be found on page 62 of the document entitled [A Guide to the Control of Respiratory Infection Outbreaks in Long-Term Care Homes](#).<sup>2</sup>

## What is the evidence that influenza antiviral medications are effective?

### ***Duration of symptoms***

When oseltamivir is used for treatment, it decreases the duration of symptoms by:

- almost 17 hours in adults and 29 hours in children based on a meta-analysis of randomized trials by Jefferson et al.;<sup>3</sup> and
- 25 hours based on a meta-analysis by Dobson et al. of influenza-infected individuals using patient-level data from randomized trials where oseltamivir was given within 36 hours of illness onset.<sup>4</sup>

### ***Complications of infection***

The review by Jefferson et al. did not find an effect of oseltamivir on influenza-related complications<sup>3</sup>, which may be due to the enrollment of mostly healthy individuals who often do not develop complications.<sup>5</sup> The review by Dobson et al. noted a 44% reduction in the risk of lower respiratory tract complications requiring antibiotics and a 63% reduction in hospital admission for any cause for those receiving oseltamivir compared to those who did not.<sup>4</sup> Observational studies have also shown the benefits of neuraminidase inhibitors. A meta-analysis of individual-level data of hospitalized patients with laboratory-confirmed or clinical pandemic influenza (A/H1N1pdm09) in 2009-2010 showed a 25% decrease in the risk of death in adults given neuraminidase inhibitors compared to those who were not treated. Early treatment (within 2 days of symptom onset) showed even more benefit.<sup>6</sup>

### ***Prophylaxis***

Antiviral medications are very effective when used for prophylaxis. The review by Jefferson et al. found that oseltamivir prophylaxis reduced symptomatic influenza by 55% compared to placebo.<sup>3</sup> The Centers

for Disease Control and Prevention (CDC) in the United States state that antiviral medications are approximately 70 to 90% effective in preventing influenza.<sup>7</sup>

## Which organizations recommend influenza antiviral medications?

Antiviral medications are recommended by a number of organizations including the:

**a) Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada)**

*The Use of Antiviral Drugs for Influenza: A Foundation Document for Practitioners* (2013) provides treatment, prophylaxis and outbreak management recommendation with regard to influenza antiviral medications.

<https://www.ammi.ca/Content/Guidelines/Flu%20%28published%20version%29%20FINAL.pdf>

**b) Centers for Disease Control and Prevention (CDC)**

The CDC website provides a comprehensive overview of the use of influenza antiviral medication.

<http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>

<http://www.cdc.gov/flu/professionals/antivirals/index.htm>

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6001a1.htm>

**c) Ministry of Health and Long-Term Care**

*A Guide to the Control of Respiratory Infection Outbreaks in Long-Term Care Homes* (2015) provides guidance regarding the treatment and prophylaxis of residents of long term care facilities during influenza outbreaks, and also regarding prophylaxis of staff members of these facilities during influenza outbreaks.

[http://www.health.gov.on.ca/en/pro/programs/publichealth/flu/docs/resp\\_infectn\\_ctrl\\_guide\\_ltc\\_2015\\_en.pdf](http://www.health.gov.on.ca/en/pro/programs/publichealth/flu/docs/resp_infectn_ctrl_guide_ltc_2015_en.pdf)

**d) Infectious Diseases Society of America (IDSA)**

*Seasonal Influenza in Adults and Children— Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America* (2009) provides recommendations regarding treatment and prophylaxis of influenza using antiviral medication. <http://cid.oxfordjournals.org/content/48/8/1003.1.full.pdf+html>

Additional information is also available from your [local public health unit](#) or [Public Health Ontario](#) ([cd@oahpp.ca](mailto:cd@oahpp.ca)).

# Appendix A

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## List of conditions that increase the risk for influenza complications:

- Chronic pulmonary disease, including asthma
- Cardiovascular disease (excluding hypertension)
- Malignancy
- Chronic renal insufficiency
- Diabetes mellitus and other metabolic disease
- Anemia and hemoglobinopathies, such as sickle cell disease
- Immunosuppression due to disease or medication
- Neurologic and neurodevelopmental disorders
- Children younger than 5 years of age
- Individuals 65 years of age or older
- People of any age who live in nursing homes or other chronic care facilities
- Pregnant women and up to 4 weeks post-partum
- Individuals < 18 years of age who are on chronic aspirin therapy, due to the risk of Reye's syndrome related to influenza
- Morbid obesity (BMI  $\geq$  40) or a BMI > 3 z-scores above the mean for age and gender
- Indigenous peoples

### Sources for list of conditions that increase the risk of influenza complications:

- [AMMI Canada Guidelines](#) - Table 3<sup>1</sup>
- [National Advisory Committee on Immunization \(NACI\). Statement on Seasonal Influenza Vaccine for 2016-2017.](#) Table 1<sup>8</sup>

# References

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