2010-2011

Influenza Antiviral Medications: A Summary for Clinicians

Antiviral medications with activity against influenza viruses are an important adjunct to influenza vaccine in the control of influenza.

- Influenza antiviral prescription drugs can be used to **treat** influenza or to **prevent influenza**.
- Two FDA-approved influenza antiviral medications are recommended for use in the United States during the 2010-2011 influenza season: **oseltamivir** (Tamiflu®) and **zanamivir** (Relenza®).
- Oseltamivir and zanamivir are chemically related antiviral medications known as neuraminidase inhibitors that have activity against both influenza A and B viruses.

Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza, 2010-2011 Influenza Season

Antiviral agent	Activity against	Use	FDA approved for	Not recommended for use in (Contraindications)	Side Effects
Zanamivir (Relenza®)	Influenza A and B	Treatment	7 yrs and older	people with underlying respiratory disease (e.g., asthma, COPD) or heart disease	**Allergic reactions**: oropharyngeal or facial edema. **Side Effects**: diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infections.
		Chemo-prophylaxis	5 yrs and older		
Oseltamivir (Tamiflu®)	Influenza A and B	Treatment	1 yr and older	none	**Side Effects**: nausea, vomiting. Transient neuropsychiatric events (self injury or delirium) mainly reported among Japanese adolescents and adults.
		Chemo-prophylaxis	1 yr and older	none	

Treatment:

When started within the first **two days** of onset of influenza illness, an influenza antiviral medication can reduce illness severity and shorten the duration of fever and symptoms. In clinical trials conducted among previously healthy outpatients with uncomplicated influenza, treatment with neuraminidase inhibitor antiviral drugs was found to reduce illness by 1-2 days. Studies indicate that influenza antiviral medications may also reduce the risk of serious influenza-related complications (e.g., pneumonia, respiratory failure, exacerbation of chronic diseases and death). When clinically indicated, influenza antiviral medications should be started **as soon as possible after** symptom onset, ideally within 48 hours of symptom onset. **Treatment should not wait for laboratory confirmation of influenza**.

Antiviral treatment started after 48 hours of symptom onset may still be beneficial in patients with severe or progressive illness, such as among persons hospitalized with influenza-related illness. Recent data indicate benefit of treatment with a neuraminidase inhibitor for people at higher risk for influenza complications or people with more severe illness in preventing influenza-related complications and deaths, even when started more than 48 hours after illness onset. For example, treatment of pregnant women

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with influenza has been shown to be most beneficial in preventing respiratory failure and death when started within less than 3 days of illness onset, but still provided benefit when started 3 through 4 days after onset compared to 5 or more days (Siston, et al JAMA 2009).

The following recommendations provide clinical indications of how neuraminidase inhibitor antiviral medications can be used to treat influenza when influenza activity is present in your community.

I. Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who:

- Has severe, complicated, or progressive illness, or
- Is hospitalized, or
- Is at higher risk for influenza complications as follows:
    - Children younger than 2 years old;*
        - Although all children younger than 2 years of age are at risk for severe complications from influenza, the risk is highest among young infants aged less than 6 months old. Because many children with mild febrile respiratory illness may have other viral infections (e.g., RSV, rhinovirus, parainfluenza, metapneumovirus virus), knowledge about other respiratory viruses as well as influenza virus strains circulating in the community is important for treatment decisions.**
    - Adults 65 years and older;
    - Persons with the following conditions:
        - chronic pulmonary (including asthma),
        - cardiovascular (except hypertension),
        - renal,
        - hepatic,
        - hematological (including sickle cell disease),
        - neurological and neurodevelopmental conditions [including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury],
        - or metabolic disorders (including diabetes mellitus);
    - Immunosuppression, including that caused by medications or by HIV infection;
    - Women who are pregnant or post-partum (within two weeks after delivery);
    - Persons younger than 19 years of age who are receiving long-term aspirin therapy;
    - American Indians and Alaskan Natives;
    - Persons who are morbidly obese (body-mass index ≥40);
    - Residents of nursing homes and other chronic-care facilities.

II. Clinical judgment, based on the patient's disease severity and progression, age, underlying medical conditions, likelihood of influenza, and time since onset of symptoms, is important to consider when making antiviral treatment decisions for high-risk outpatients. When indicated, antiviral treatment should be started as soon as possible after illness onset.

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- The greatest benefit is when antiviral treatment is started within 48 hours of influenza illness onset.
- Antiviral treatment may still be beneficial in patients with severe, complicated, or progressive illness, and in hospitalized patients when administered more than 48 hours from illness onset.

III. Antiviral treatment also can be considered for any previously healthy, non high risk, symptomatic outpatient with confirmed or suspected influenza based upon clinical judgment, if treatment can be initiated within 48 hours of illness onset.

Note: Recommended antiviral medications (neuraminidase inhibitors) are not licensed for treatment of children <1 year of age for oseltamivir or children aged <7 years for zanamivir. Oseltamivir was used for treatment of 2009 pandemic influenza A (H1N1) virus infection in children <1 year of age under an Emergency Use Authorization (EUA), but this EUA has expired. Limited information on use of oseltamivir for children from birth to 1 year is available.

*While children aged <5 years are considered to be at higher risk for influenza-related complications, the risk is highest among children aged <2 years old.

**The likelihood of influenza virus infection in a patient depends upon the prevalence of influenza activity in the local community, and the patient's signs and symptoms. Information about influenza activity in the United States during the influenza season is available at www.cdc.gov/flu and http://www.cdc.gov/flu/weekly/fluactivitysurv.htm. For information on local community influenza activity, clinicians should contact their local and state health departments.

Confirmation of influenza virus infection may be performed by different influenza testing methods. Information on influenza testing is available at: www.cdc.gov/flu/professionals/diagnosis/.

In areas with limited antiviral medication availability, local public health authorities might provide additional guidance about prioritizing treatment within groups at higher risk for complications. Current CDC guidance on treatment of influenza should be consulted, and updated recommendations from CDC can be found at http://www.cdc.gov/flu/.

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Recommended Dosage and Duration of Treatment or Chemoprophylaxis for Influenza Antiviral Medications, 2010-2011 Influenza Season

Antiviral Agent	Use	Children	Adults
Zanamivir (Relenza®)	**Treatment**	10 mg (2 inhalations) **twice** daily	10 mg (2 inhalations) **twice** daily
	Chemo prophylaxis	10 mg (2 inhalations) **once** daily	10 mg (2 inhalations) **once** daily
Oseltamivir (Tamiflu®)	**Treatment**	**(Not FDA approved for use in children <1 yr old, but was approved under EUA during the 2009 H1N1 pandemic)** If <1 yr old, the dose is 3 mg/kg/dose **twice** daily	75 mg **twice** daily
		(Dose varies by child's weight) If ≥1 yr old and weigh 15 kg or less, the dose is 30 mg **twice** a day.	
		If ≥1 yr old and weigh >15 to 23 kg, the dose is 45 mg **twice** a day.	
		If ≥1 yr old and weigh >23 to 40 kg, the dose is 60 mg **twice** a day.	
		If ≥1 yr old and weigh more than 40 kg, the dose is 75 mg **twice** a day.	
	Chemo prophylaxis	**(Not FDA approved for use in children <1 yr old)** If child is <3 months old, chemoprophylactic use is not recommended unless situation is judged critical due to limited data on use in this age group.	75 mg **once** daily
		(Not FDA approved for children <1 yr, but use in children ≥3 months and <1 yr old was approved under EUA during the 2009 H1N1 pandemic) If child ≥3 months and <1 yr old, dose is 3 mg/kg/dose **once** per day.	
		(Dose varies by child's weight) If ≥1 yr old, and weigh 15 kg or less, the dose is 30 mg **once** a day.	
		If ≥1 yr old and weigh >15 to 23 kg, the dose is 45 mg **once** a day.	
		If ≥1 yr old and weigh >23 to 40 kg, the dose is 60 mg **once** a day.	
		If ≥1 yr old and weigh more than 40 kg, the dose is 75 mg **once** a day.	

Duration of Treatment or Chemoprophylaxis

Treatment	Recommended duration for antiviral treatment is 5 days. Longer treatment courses for patients who remain severely ill after 5 days of treatment can be considered.
Chemo prophylaxis	Recommended duration is 7 days after exposure.
	For control of outbreaks in long-term care facilities and hospital, CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks, including in vaccinated persons, and up to 1 week after the last known case was identified.

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Chemoprophylaxis:

Annual influenza vaccination is the best way to prevent influenza because vaccination can be given well before influenza virus exposures occur, and can provide safe and effective immunity throughout the influenza season. However, antiviral medications are **70%** to **90%** effective in preventing influenza and are useful adjuncts to vaccination. To be effective as chemoprophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza or until immunity after vaccination develops (antibody development after vaccination takes about **two weeks** in adults and can take longer in children depending on age and vaccination history). Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last exposure to an infectious person. Patients receiving chemoprophylaxis should be encouraged to seek medical evaluation as soon as they develop a febrile respiratory illness that might indicate influenza. CDC does not recommend widespread or routine use of antiviral medications for chemoprophylaxis so as to limit the possibilities that antiviral resistant viruses could emerge. Indiscriminate use of chemoprophylaxis might promote resistance to antiviral medications, or reduce antiviral medication availability for treatment of persons at higher risk for influenza complications or those who are severely ill. **An emphasis on early treatment and monitoring is an alternative to chemoprophylaxis after a suspected exposure for some persons**.

However, prophylactic use of antiviral medications to control outbreaks among high risk persons in institutional settings is recommended. For example, when influenza is identified as a cause of respiratory outbreak among nursing home residents, use of prophylaxis for all residents and for unvaccinated health care staff is recommended. For more information on the control of institutional outbreaks, please see the IDSA guidelines www.idsociety.org/content.aspx?id=9202#flu

The following are examples of how antiviral medications can be considered for chemoprophylaxis to prevent influenza:

- Prevention of influenza in persons at high risk of influenza complications during the first two weeks following vaccination after exposure to an infectious person.
- Prevention for people with severe immune deficiencies or others who might not respond to influenza vaccination, such as persons receiving immunosuppressive medications, after exposure to an infectious person
- Prevention for people at high risk for complications from influenza who cannot receive influenza vaccine due to a severe egg allergy or other contraindication after exposure to an infectious person.
- Prevention of influenza among residents of institutions, such as long-term care facilities, during influenza outbreaks in the institution. For more information, see IDSA guidelines: www.idsociety.org/content.aspx?id=9202#flu.

Side Effects:

- When considering use of influenza antiviral medications, clinicians must consider the patient's age, weight and renal function; presence of other medical conditions; indications for use (i.e., chemoprophylaxis or therapy); and the potential for interaction with other medications.
- For more information on safety, effectiveness and dosing for oseltamivir and zanamivir, visit www.cdc.gov/flu/professionals/antivirals/index.htm or consult the package inserts.

For more information, visit www.cdc.gov/flu, or call CDC at 800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

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