Influenza Antiviral Medications: Summary for Clinicians

The information on this page should be considered current for the 2014-2015 influenza season for clinical practice regarding the use of influenza antiviral medications.

This page contains excerpts from Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza - Recommendations of the Advisory Committee on Immunization Practices (ACIP). PDF Version[1 MB, 28 pages]

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**.
- Four licensed prescription influenza antiviral agents are available in the United States.
    - Two FDA-approved influenza antiviral medications are recommended for use in the United States during the 2014-2015 influenza season: oral **oseltamivir** (Tamiflu®) and inhaled **zanamivir** (Relenza®). Oseltamivir and zanamivir are chemically related antiviral medications known as neuraminidase inhibitors that have activity against both influenza A and B viruses.
    - Amantadine and rimantadine are antiviral drugs in a class of medications known as adamantanes. These medications are active against influenza A viruses, but not influenza B viruses. As in recent past seasons, there continues to be high levels of resistance (>99%) to adamantanes among influenza A (H3N2) and influenza A (H1N1) pdm09 ("2009 H1N1") viruses. Therefore, amantadine and rimantadine are not recommended for antiviral treatment or chemoprophylaxis of currently circulating influenza A viruses.
- Antiviral resistance to oseltamivir and zanamivir among circulating influenza viruses is currently low, but this can change. Also, antiviral resistance can emerge during or after treatment in some patients (e.g., immunosuppressed).
    - For information about antiviral drug resistance to influenza viruses and guidance on the use of influenza antiviral medications when antiviral resistance is suspected or documented this season, see Antiviral Drug-Resistance among Influenza Viruses(http://wwwdev.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm).
    - For weekly surveillance data on antiviral resistance this season, see the FluView U.S. Influenza Surveillance Report(http://wwwdev.cdc.gov/flu/weekly/index.htm).

Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza

Antiviral Agent	Activity Against	Use	Recommended For	Not Recommended for Use in	Adverse Events
Oseltamivir (Tamiflu®)	**Influenza A and B**	**Treatment**	Any age[1]	N/A	**Adverse events:** nausea, vomiting. Sporadic, transient neuropsychiatric events (self-injury or delirium) mainly reported among Japanese adolescents and adults.
		Chemo-prophylaxis	3 months and older[1]	N/A	
Zanamivir[4] (Relenza®)	**Influenza A and B**	**Treatment**	7 yrs and older	people with underlying respiratory disease (e.g., asthma, COPD)[2]	**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.
		Chemo-prophylaxis	5 yrs and older	people with underlying respiratory disease (e.g., asthma, COPD)[2]	

[1] Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza in persons 14 days and older, and for chemoprophylaxis in persons 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year of age, is recommended by the CDC and the American Academy of Pediatrics. If a child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless the situation is judged critical due to limited data in this age group.

[2] Relenza is contraindicated in patients with history of allergy to milk protein.

Summary of Influenza Antiviral Treatment Recommendations

- Clinical trials and observational data show that early antiviral treatment can shorten the duration of fever and illness symptoms, and may reduce the risk of complications from influenza (e.g., otitis media in young children, pneumonia, and respiratory failure).
- Early treatment of hospitalized patients can reduce death.
- In hospitalized children, early antiviral treatment has been shown to shorten the duration of hospitalization.
- Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of influenza illness onset.
- Antiviral treatment is recommended **as early as possible** for any patient with confirmed or suspected influenza who:
    - is hospitalized;
    - has severe, complicated, or progressive illness; or
    - is at higher risk for influenza complications.
- Persons at higher risk for influenza complications recommended for antiviral treatment include:
    - children aged younger than 2 years;*
    - adults aged 65 years and older;
    - persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment 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);
    - persons with immunosuppression, including that caused by medications or by HIV infection;
    - women who are pregnant or postpartum (within 2 weeks after delivery);
    - persons aged younger than 19 years who are receiving long-term aspirin therapy;
    - American Indians/Alaska Natives;
    - persons who are morbidly obese (i.e., body mass index is equal to or greater than 40); and
    - residents of nursing homes and other chronic care facilities.

(Adapted from Fiore, 2011, Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza - Recommendations of the Advisory Committee on Immunization Practices (ACIP). PDF Version)

- Clinical judgment, on the basis of the patient's disease severity and progression, age, underlying medical conditions, likelihood of influenza, and time since onset of symptoms, is important when making antiviral treatment decisions for high-risk outpatients.
- When indicated, antiviral treatment should be started as soon as possible after illness onset, ideally within 48 hours of symptom onset. However, antiviral treatment might have some benefits in patients with severe, complicated or progressive illness, and in hospitalized patients when started after 48 hours of illness onset.
    - Observational studies in hospitalized patients with influenza have reported that clinical benefit is greatest when oseltamivir is started within 48 hours of illness onset (Hsu, 2012; Louie, 2013; Muthuri, 2013). However, some studies suggest that antiviral treatment might still be beneficial in hospitalized patients when started 4 and 5 days after illness onset (Louie, 2012; Yu, 2011). Antiviral treatment of pregnant women (of any trimester) with influenza A (2009 H1N1) virus infection 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 3–4 days after onset compared to 5 or more days (Siston, 2010).
- **Decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza** (see section on Diagnostic Testing for Influenza).
- While influenza vaccination is the first and best way to prevent influenza illness, a history of influenza vaccination does not rule out the possibility of influenza virus infection in an ill patient with clinical signs and symptoms compatible with influenza.
- Antiviral treatment also can be considered for any previously healthy, symptomatic outpatient not at high risk with confirmed or suspected influenza on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.†
    - One randomized clinical trial in children with uncomplicated influenza demonstrated a modest reduction in duration of symptoms and virus shedding in patients initiating treatment after 48 hours; post hoc analysis suggested that treatment initiated 72 hours after illness onset reduced symptoms by one day compared with placebo (Fry, 2014).
- Oral oseltamivir is preferred for treatment of pregnant women (Rasmussen, 2009; 2011). Pregnant women are recommended to receive the same antiviral dosing as non-pregnant persons. See Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza(http://wwwdev.cdc.gov/flu/professionals/antivirals/avrec_ob.htm) for additional information.

- On December 21, 2012, the U.S. Food and Drug Administration (FDA) approved the antiviral medication oseltamivir (Tamiflu®) for the treatment of influenza in people aged 14 days and older. An FDA press release related to this announcement is available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333205.htm.

Treatment Considerations for Patients Hospitalized with Suspected or Confirmed Influenza

Treatment of patients with severe influenza (e.g., those requiring hospitalization) presents multiple challenges. The effect of specific antiviral strategies in serious or life-threatening influenza is not established from clinical trials conducted to support licensure of oral oseltamivir and inhaled zanamivir, as those studies were conducted primarily among previously healthy outpatients with uncomplicated illness. However, a number of observational studies have reported that oral oseltamivir treatment started 4 and 5 days after illness onset of patients hospitalized with suspected or confirmed influenza is associated with lower risk for severe outcomes (EH Lee, 2010; N Lee, 2008; N Lee, 2010; Louie, 2012; McGreer, 2007; Siston, 2010). For this reason, the following recommendations do not necessarily represent FDA-approved uses of antiviral products, but are based on published expert opinion and observational studies and are subject to change as the developmental status of investigational products and the epidemiologic and virologic features of influenza change over time.

- Initiation of antiviral treatment as early as possible is recommended for hospitalized patients. However, antiviral treatment might be effective in reducing morbidity and mortality in hospitalized patients even if treatment is not started until more than 48 hours after onset of illness.
- For hospitalized patients and patients with severe or complicated illness, treatment with oral or enterically administered oseltamivir is recommended. Inhaled zanamivir is not recommended because of the lack of data for use in patients with severe influenza disease.
- The recommended treatment course for uncomplicated influenza is two doses per day of a neuraminidase inhibitor medication for 5 days; however, the optimal duration and dose are uncertain for severe or complicated influenza. Treatment regimens might need to be altered to fit the clinical circumstances. For example, clinical judgment should be the guide regarding the need to extend treatment regimens longer than 5 days for patients whose illness is prolonged. Critically ill patients with respiratory failure can have prolonged influenza viral replication in the lower respiratory tract.
    - Clinical judgment and virologic testing of lower respiratory tract specimens by real-time reverse transcription-polymerase chain reaction (RT-PCR) should guide decisions to consider treatment regimens longer than 5 days for patients with severe and prolonged illness. For patients with

lower respiratory tract disease, lower respiratory tract specimens, such as bronchoalveolar lavage fluid or endotracheal aspirates, are preferred; an oropharyngeal (throat) swab may be collected if lower respiratory specimens are not available. Testing of lower respiratory tract specimens may yield the diagnosis when testing of upper respiratory tract specimens is negative. Multiple respiratory tract specimens collected on different days should be tested if influenza virus infection is suspected but a definitive diagnosis has not been made.

- Longer treatment regimens might be necessary in immunosuppressed persons who may have prolonged influenza viral replication. Such patients are at risk of developing antiviral-resistant virus.
- A higher dose of oral or enterically administered oseltamivir has been recommended by some experts (e.g., 150 mg twice daily in adults with normal renal function) for treatment of influenza in immunocompromised patients and in severely ill hospitalized patients. However, oral or enterically administered oseltamivir has been reported to be adequately absorbed in critically ill adults, with standard doses producing therapeutic blood levels (Ariano, 2010), and limited data suggest that higher dosing may not provide additional clinical benefit (Abdel-Ghafar, 2008; Ariano, 2010; Kumar, 2010; Lee, 2013; South East Asia Infectious Disease Clinical Research Network, 2013). Studies indicate that the exposure to oseltamivir carboxylate (the active metabolite of oseltamivir) is similar between obese and non-obese subjects for both 75 mg and 150 mg doses given twice daily (Ariano, 2010; Jittamala, 2014; Pai, 2011; Thorne-Humphrey, 2011).

- Limited data suggest that oseltamivir administered orally or by oro/naso gastric tube is well absorbed in critically ill influenza patients, including those in the intensive care unit, on continuous renal replacement therapy, and/or on extracorporeal membrane oxygenation (Ariano, 2010; Eyler, 2012a; Eyler, 2012b; Giraud, 2011; Kromdijk, 2013; Lemaitre, 2012; Mulla, 2013; Taylor, 2008). However, for patients who cannot tolerate or absorb oral or enterically-administered oseltamivir because of suspected or known gastric stasis, malabsorption, or gastrointestinal bleeding, the use of investigational intravenous (IV) zanamivir should be considered. IV zanamivir is an investigational parenterally administered neuraminidase inhibitor product available only either by enrollment in an ongoing phase III clinical trial, or under an emergency investigational new drug (EIND) request to the manufacturer for compassionate use in hospitalized adult and pediatric patients with severe influenza. (See Intravenous Influenza Antiviral Medications and CDC Considerations Related to Investigational Use of Intravenous Zanamivir for 2014-2015 Influenza Season(http://wwwdev.cdc.gov/flu/professionals/antivirals/intravenous-antivirals.htm).)

- It is possible that some influenza viruses may become resistant to oseltamivir during antiviral treatment and remain susceptible to zanamivir; this has been reported most often for influenza A H1N1 viruses (Graitcer, 2011; Lackenby, 2011). Resistance of influenza viruses to antiviral drugs can also occur spontaneously, with no known exposure to antiviral medications (Hurt, 2011; Takashita, 2014). If a hospitalized patient treated with oseltamivir manifests progressive lower respiratory symptoms, resistant virus should be considered. In view of the limited alternatives, CDC recommends that investigational use of IV zanamivir should be considered for treatment of severely ill patients with oseltamivir-resistant virus infection (Dulek, 2010; Gaur, 2010; Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza, 2010). Oseltamivir should not be stopped until IV zanamivir can be initiated. However, clinicians should note that failure to improve or clinical deterioration during oseltamivir treatment is more likely to be related to the natural history of acute lung injury and inflammatory damage or onset of other complications (e.g. renal failure, septic shock, ventilator-associated pneumonia) than to emergence of oseltamivir resistance. Severely immunosuppressed persons (e.g. hematopoietic stem cell transplant recipients) are at highest risk for emergence of oseltamivir-resistant influenza virus infection during or following oseltamivir treatment (Hurt, 2012). Molecular assays can detect genetic changes in influenza viruses associated with oseltamivir resistance. The CDC Influenza Division is available for consultation as needed.
- Careful attention to ventilator and fluid management and to the prevention and treatment of secondary bacterial pneumonia (e.g., *S. pneumoniae*, *S. pyogenes*, and *S. aureus*, including MRSA) also is critical for severely ill patients (Bautista, 2010; Finelli, 2008; Hageman, 2006; Harper, 2009; Mandell, 2007; Mauad, 2010; Shieh, 2010).

Diagnostic Testing for Influenza

- Rapid Influenza Diagnostic Tests (RIDTs)(http://wwwdev.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm) can be useful to identify influenza virus infection as a cause of respiratory outbreaks in any setting. RIDTs are antigen detection tests and produce very quick results, but the results may not be accurate. A recent meta-analysis evaluating 159 studies of 26 RIDTs compared with a reference standard of either RT-PCR or viral culture reported a pooled sensitivity of 62.3% (95% CI, 57.9% to 66.6%) and pooled specificity of 98.2% (CI, 97.5% to 98.7%), although sensitivities as low as 10% were reported in individual studies, depending on characteristics such as specimen type, age of patient, and virus detected (Chartrand, 2012).

    - Sensitivities were generally lower in adults (53.9% [95% CI, 47.9% to 59.8%]) than in children (66.6% [95% CI, 61.6% to 71.7%]), and lower for influenza B (52.2% [95% CI, 45.0% to 59.3%]) than influenza A (64.6% [95% CI, 59.0% to 70.1%]) (Chartrand, 2012). Sensitivities were also lower when compared with RT-PCR as the reference standard (53.9% [95% CI, 48.2% to 59.6%]) versus viral culture (72.3% [95% CI, 66.8% to 77.9%]) (Chartrand, 2012).
    - In the meta-analysis, RIDTs did not perform markedly worse in the 35% of studies conducted during the 2009 H1N1 pandemic (Chartrand, 2012). RIDT sensitivity of 58% was reported on respiratory specimens from 24 fatal cases of influenza A from the 2013-2014 season (Ayscue, 2014). Sensitivity in lower respiratory tract samples may be even lower than upper respiratory samples; in one study, RIDTs were positive in only five (25%) of 20 bronchoscopic samples in patients with severe 2009 H1N1 virus infection requiring mechanical ventilation (Blyth, 2009).
- False negative results occur more commonly than false positive results. In particular, false negative test results are common during influenza season. Additionally, other antigen detection tests (e.g. immunofluorescence assays) also lack sensitivity compared to RT-PCR. Clinicians should realize that **a negative RIDT or immunofluorescence (e.g. direct florescent antibody staining - DFA) result does NOT exclude a diagnosis of influenza** in a patient with suspected influenza. When there is clinical suspicion of influenza and antiviral treatment is indicated, antiviral treatment should be started as soon as possible without waiting for results of additional influenza testing.
- Other testing (i.e., RT-PCR, viral culture) is much more accurate, but can take longer. When influenza is suspected and antiviral treatment is indicated, antiviral treatment should begin as soon as possible and should not wait for the results of testing.
- Rapid molecular assays are a new type of molecular influenza diagnostic test. Currently, there is only one rapid molecular assay that is FDA-approved for use in the United States. Additional rapid molecular assays may become available in the future. As with other molecular diagnostic tests, if influenza is suspected and treatment is clinically indicated, antiviral treatment should begin as soon as possible and should not wait for the results of testing.

To Minimize False RIDT Results

- Collect specimens as early in the illness as possible (ideally less than 4 days from illness onset).
- Follow manufacturer's instructions, including acceptable specimens, and handling.
- Follow-up negative results with confirmatory tests (i.e., RT-PCR or viral culture) if a laboratory-confirmed influenza diagnosis is desired.

Information on Local Influenza Activity

- Clinicians should contact their local or state health department for information about current influenza activity. For more information about influenza activity in the United States during the influenza season, visit the Weekly U.S. Influenza Surveillance Report (FluView).
- **For more information on influenza diagnostic testing**, see Clinical Description & Lab Diagnosis of Influenza(http://wwwdev.cdc.gov/flu/professionals/diagnosis/index.htm).

Table 2. Recommended Dosage and Duration of Influenza Antiviral Medications for Treatment or Chemoprophylaxis

Antiviral Agent	Use	Children	Adults
Oseltamivir (Tamiflu®)	**Treatment (5 days)**	**If younger than 1 yr old**[1]: 3 mg/kg/dose twice daily[2,3] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **twice** a day >15 to 23 kg, the dose is 45 mg **twice** a day >23 to 40 kg, the dose is 60 mg **twice** a day >40 kg, the dose is 75 mg **twice** a day	75 mg **twice** daily
	Chemo-prophylaxis (7 days)	If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical due to limited data in this age group. **If child is 3 months or older and younger than 1 yr old**[1] 3 mg/kg/dose once daily[2] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **once** a day >15 to 23 kg, the dose is 45 mg **once** a day >23 to 40 kg, the dose is 60 mg **once** a day >40 kg, the dose is 75 mg **once** a day	75 mg **once** daily

Zanamivir[4] (Relenza®)	**Treatment (5 days)**	10 mg (two 5-mg inhalations) **twice** daily (**FDA approved and recommended for use in children 7 yrs or older**)	10 mg (two 5-mg inhalations) **twice** daily
	Chemo-prophylaxis (7 days)	10 mg (two 5-mg inhalations) **once** daily (**FDA approved for and recommended for use in children 5 yrs or older**)	10 mg (two 5-mg inhalations) **once** daily

1 Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza with twice-daily dosing in persons 14 days and older, and for chemoprophylaxis with once-daily dosing in persons 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year of age, is recommended by the CDC and the American Academy of Pediatrics (Committee on Infectious Diseases, 2013).

2 This is the FDA-approved oral oseltamivir treatment dose for infants 14 days and older and less than 1 year old, and provides oseltamivir exposure in children similar to that achieved by the approved dose of 75 mg orally twice daily for adults, as shown in two studies of oseltamivir pharmacokinetics in children (Kimberlin, 2013 [CASG 114], EU study WP22849, FDA Clinical Pharmacology Review). The American Academy of Pediatrics has recommended an oseltamivir treatment dose of 3.5 mg/kg orally twice daily for infants aged 9-11 months for the 2013-14 season, on the basis of data which indicated that a higher dose of 3.5 mg/kg was needed to achieve the protocol-defined targeted exposure for this cohort as defined in the CASG 114 study (Kimberlin, 2013). It is unknown whether this higher dose will improve efficacy or prevent the development of antiviral resistance. However, there is no evidence that the 3.5 mg/kg dose is harmful or causes more adverse events to infants in this age group.

3 Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants might have slower clearance of oral oseltamivir because of immature renal function, and doses recommended for full-term infants might lead to very high drug concentrations in this age group. CDC recommends dosing as also recommended by the American Academy of Pediatrics (Committee on Infectious Diseases, 2013): limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provide the basis for dosing preterm infants using their postmenstrual age (gestational age + chronological age): 1.0 mg/kg/dose, orally, twice daily, for those <38 weeks postmenstrual age; 1.5 mg/kg/dose, orally, twice daily, for those 38 through 40 weeks postmenstrual age; 3.0 mg/kg/dose, orally, twice daily, for those >40 weeks postmenstrual age.

4 Inhaled zanamivir is approved for treatment of acute uncomplicated influenza with twice-daily dosing in persons aged 7 years and older, and for chemoprophylaxis with once-daily dosing in persons aged 5 years and older.

Table 3. 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 last known exposure).
	For control of outbreaks in institutional settings (e.g. long-term care facilities for elderly persons and children) and hospitals, CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks, and continuing up to 1 week after the last known case was identified. Antiviral chemoprophylaxis should be considered for all exposed residents, including those who have received influenza vaccination, and for unvaccinated institutional employees.

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.
- Antiviral medications are approximately **70%** to **90%** effective in preventing influenza and are useful adjuncts to influenza vaccination.
- 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.
- In general, CDC does not recommend seasonal or pre-exposure antiviral chemoprophylaxis, but antiviral medications can be considered for chemoprophylaxis in certain situations.
- **The following are examples of situations where 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 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 web site[259 KB, 30 pages].

- **An emphasis on close monitoring and early initiation of antiviral treatment if fever and/or respiratory symptoms develop is an alternative to chemoprophylaxis after a suspected exposure for some persons.**
- To be effective as chemoprophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza and continued for 7 days after the last known exposure. For persons taking antiviral chemoprophylaxis after inactivated influenza vaccination, the recommended duration is 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).**
- **Antiviral chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the first exposure to an infectious person.**
- **Patients receiving antiviral chemoprophylaxis should be encouraged to seek medical evaluation as soon as they develop a febrile respiratory illness that might indicate influenza.**

Special Considerations for Institutional Settings

Use of antiviral chemoprophylaxis to control outbreaks among high risk persons in institutional settings is recommended. An influenza outbreak is likely when at least two residents are ill within 72 hours, and at least one has laboratory confirmed influenza. When influenza is identified as a cause of a respiratory disease outbreak among nursing home residents, use of antiviral medications for chemoprophylaxis is recommended for residents (regardless of whether they have received influenza vaccination) and for unvaccinated health care personnel. For newly-vaccinated staff, antiviral chemoprophylaxis can be administered up to two weeks (the time needed for antibody development) following influenza vaccination. Chemoprophylaxis may also be considered for all employees, regardless of their influenza vaccination status, if the outbreak is caused by a strain of influenza virus that is not well-matched by the vaccine. Antiviral chemoprophylaxis should be administered for a minimum of two weeks, and continue for at least seven days after the last known case was identified. For more information on the control of

institutional outbreaks, please see CDC's Interim Guidance for Influenza Outbreak Management in Long-Term Care Facilities(http://wwwdev.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm) and the IDSA guidelines web site[259 KB, 30 pages].

Adverse Events

- 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 oral oseltamivir and inhaled zanamivir, visit Antiviral Drugs(http://wwwdev.cdc.gov/flu/professionals/antivirals/index.htm) or consult the package inserts.

Footnotes

* Although all children aged younger than 5 years are considered at higher risk for complications from influenza, the highest risk is for those aged younger than 2 years, with the highest hospitalization and death rates among infants aged younger than 6 months. Because many children with mild febrile respiratory illness might have other viral infections (e.g., respiratory syncytial virus, rhinovirus, parainfluenza virus, or human metapneumovirus), knowledge of other respiratory viruses as well as influenza virus strains circulating in the community is important for treatment decisions. The likelihood of influenza virus infection in a patient depends on the prevalence of influenza activity in the local community and on the patient's signs and symptoms. Information about influenza activity in the United States is available at FluView. For information on local community influenza activity, clinicians should contact their local and state health departments.

† Recommended antiviral medications (neuraminidase inhibitors) are licensed by the FDA for treatment of children aged 14 days and older (oral oseltamivir) and for those aged 7 years and older (inhaled zanamivir). Oseltamivir was used for treatment of 2009 pandemic influenza A (H1N1) virus infection in children aged younger than 1 year under an Emergency Use Authorization, which expired on June 23, 2010. Limited information regarding use of oral oseltamivir for children from birth through age 1 year is available; however, the use of oseltamivir for treatment is recommended by the CDC and the American Academy of Pediatrics for children of any age. Confirmation of influenza virus infection may be performed by different influenza testing methods. Information on influenza testing is available at Clinical Description & Lab Diagnosis of Influenza(http://wwwdev.cdc.gov/flu/professionals/diagnosis/index.htm). 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; updated recommendations from CDC are available on the Seasonal Influenza (Flu)(http://wwwdev.cdc.gov/flu/index.htm) site, and the ACIP antiviral recommendations[1 MB, 28 pages].

For more information, visit the Seasonal Influenza (Flu)(http://wwwdev.cdc.gov/flu/index.htm) site, or call CDC at 800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

Selected References

- *References noted in this summary are not complete. A more comprehensive list of influenza antiviral references can be found at Antiviral Guide References*(http://wwwdev.cdc.gov/flu/professionals/antivirals/antiviral-mmwr-references.htm).

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