ANTIVIRAL AGENTS FOR THE PREVENTION AND CONTROL OF INFLUENZA

Clinician Outreach and Communication Activity (COCA) Conference Call

November 23, 2010

Office of Public Health Preparedness and Response
Division of Emergency Operations

Objectives

At the conclusion of this hour, each participant should be able to:

- List currently recommended influenza antiviral medications
- Describe the effectiveness and safety of influenza antiviral medications
- Understand current recommendations for the use of antiviral medications to treat and prevent influenza during the current season

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TODAY'S PRESENTER

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Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza

Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010

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National Center for Immunization & Respiratory Diseases
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Introduction

Primary changes and updates in the recommendations

- Antiviral treatment is recommended as soon as possible for:
  - Patients with confirmed or suspected influenza who are hospitalized, or have severe, complicated or progressive illness
  - Outpatients with confirmed or suspected influenza who are at higher risk for influenza complications based on their age and/or medical conditions
    - Clinical judgment should be an important component of outpatient treatment decisions
- Recommended antiviral medications are oseltamivir and zanamivir
  - Based on recent viral surveillance and resistance data indicating that >99% of currently circulating influenza virus strains are sensitive to these medications
- Oseltamivir should be used to provide treatment or chemoprophylaxis for infants younger than one year old, when indicated

Introduction

Primary changes and updates in the recommendations (continued)

- Because antiviral resistance patterns may change over time, clinicians should monitor local influenza antiviral resistance surveillance data
- Antiviral treatment can be considered for any previously healthy non high risk symptomatic outpatient with confirmed or suspected influenza who is not in the recommended groups, based upon clinical judgment, if treatment can be initiated within 48 hours of illness onset

Influenza Virus Transmission

- **Large particle respiratory droplet transmission**
  - Traditionally thought to be the primary mode of person-to-person spread (infected person coughing, sneezing close to a susceptible person)
  - Droplets travel short distance (within about 6 ft) – do not remain suspended in the air – close contact required
- **Relative contribution of different transmission modes unclear; other possible transmission modalities:**
  - Airborne transmission via small particle aerosols in the vicinity of the infectious individual
  - Indirect contact via hand transfer of influenza virus from virus-contaminated surfaces objects to mucosal surfaces of the face (e.g., nose, mouth)
- Airborne transmission over longer distances, such as from one patient room to another has not been documented and is thought *not to occur*

Influenza Virus Transmission

Incubation period: 1-4 days (average: 2 days)

Serial interval: estimated 3-4 days among household contacts

Influenza viral shedding:

Adults: day before symptoms begin through 5-7days after illness onset

Young children: several days before illness onset is possible through 10 or more days after onset of symptoms

Immunocompromised or severely immunosuppressed persons: weeks to months has been documented

Clinical Signs and Symptoms

- **Asymptomatic infection can occur** (contact, household, serological studies)
- **Uncomplicated influenza illness**
  - Abrupt onset of fever, myalgia, headache, malaise, nonproductive cough, sore throat, rhinitis
  - Acute respiratory Illness without fever
  - Young children: less likely to experience typical influenza signs and symptoms (present with dehydration, irritability, poor oral intake)
    - Infants can present with fever only
  - Atypical presentations
    - Elderly may not manifest fever or classic "influenza-like illness"
    - Immunocompromised, severely immunosuppressed patients
- Difficult to identify influenza illness on clinical signs and symptoms alone
  - Multiple etiologies for acute febrile respiratory illness, especially in young children
  - ➢ *Diagnosis of influenza should be considered in patients with acute respiratory illness signs and symptoms when influenza viruses are circulating in the community*

Clinical Signs and Symptoms

- **Complications from influenza virus infections:**
  - Moderate complications: sinusitis, otitis media
  - **Exacerbation of underlying conditions** *(e.g., pulmonary or cardiac disease)*
  - **Primary influenza viral pneumonitis and pneumonia**
    - Progressing to respiratory failure and acute respiratory distress syndrome *(can be fulminant)*
    - *Vasopressor dependent shock; acute renal failure*
  - Coinfections with other viral or bacterial pathogens
  - **Secondary bacterial pneumonia and/or sepsis** *(can be fulminant)*
    - *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes*
  - Cardiac: myocarditis, pericarditis *(uncommon)*
  - Neurologic: wide range: febrile seizures to encephalopathy, acute necrotizing encephalitis, transverse myelitis, Reye's syndrome
  - Musculoskeletal: myositis, rhabdomyelitis
  - Young children: initial symptoms can mimic bacterial sepsis (high fever)
  - Severe complications can occur even among young and previously healthy persons

Risk Factors for Influenza Complications

- Children younger than 5 years old (especially aged <2 years);
- Adults 65 years of age and older;
- Persons with the following conditions:
  - chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), metabolic disorders (including diabetes mellitus), and 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];
- Immunosuppression, including that caused by medications or by HIV infection;
- Women who are pregnant or postpartum (within 2 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 equal to or greater than 40);
- Residents of nursing homes and other chronic care facilities

Role of Laboratory Diagnosis

- Diagnosis of influenza based on symptoms alone is limited; illness caused by other pathogens can be similar to influenza virus infection
- Available tests:
  - Rapid diagnostic (antigen) testing
    - Rapid influenza diagnostic tests [RIDTs] (simple, produce quick result)
    - Immunoflorescence (Direct florescent antibody staining [DFA])
  - Detection of viral RNA (not available at every clinical site or hospital)
    - Reverse transcription-polymerase chain reaction [RT-PCR]
  - Isolation of influenza virus: tissue cell viral culture (takes 3-10 days)
  - Serology (not indicated except for research/public health investigations)
- Sensitivity and specificity are test parameters, but can vary by:
  - Type of test used, type of specimen tested, quality of specimen, timing of specimen collection in relation to illness onset, lab that performs test
- Prevalence of circulating influenza viruses in the population tested varies during the season and impacts predictive values of influenza tests:
- Results should be evaluated in the context of other clinical and epidemiologic information

Role of Laboratory Diagnosis

- Acceptable specimens vary by test. Specimens should be collected as close to illness onset as possible (<3-4 days after onset)
- Nasopharyngeal and nasal specimens generally have higher yield for detection of influenza viruses than throat swab specimens
- Sensitivities of currently available RIDTs are generally low to moderate 50-70% (range 10-80%) and specificities are high
- **Negative RIDT results do not exclude influenza virus infection and should not be used to make treatment or infection control decisions**
- Only influenza virus isolates can provide detailed information on characteristics of influenza viruses (antigenic, genetic, antiviral resistance levels)
- RT-PCR is most accurate and sensitive test for detecting influenza viruses; platforms capable of subtyping influenza A viruses are available in state public health and some reference labs

Antiviral Agents for Influenza

Four licensed influenza antiviral agents in the U.S.:

- Neuraminidase inhibitors (NIs): oseltamivir (Tamiflu®) , zanamivir (Relenza®)
  - **Primary antiviral agents recommended for treatment and chemoprophylaxis**
  - **Active against both influenza A and B viruses**
  - Adverse events:
    - Oseltamivir (nausea, emesis)
    - Zanamivir (bronchospasm, contraindicated in patients with chronic pulmonary disease – asthma, COPD)
    - Both drugs: delirium, abnormal behavior reported in Japanese adolescents
- Adamantanes : amantadine, rimantadine
  - Active only against influenza A viruses, not influenza B viruses
  - **NOT RECOMMENDED** for treatment or chemoprophylaxis of influenza A
    - Widespread resistance among influenza A (H3N2) and 2009 H1N1 virus strains

Antiviral Resistance Among Influenza Viruses

- 2009 H1N1 virus strains, influenza A (H3N2) virus strains
  - Sensitivity to oseltamivir and zanamivir
  - Resistance to adamantanes
- Influenza B virus strains
  - Sensitive to oseltamivir and zanamivir
- Sporadic oseltamivir-resistant 2009 pandemic influenza A (H1N1) virus infections identified, with rare episodes of limited transmission, but public health impact has been limited to date
  - Additional sporadic cases of oseltamivir-resistant 2009 H1N1 virus infections expected
  - Ongoing surveillance for oseltamivir-resistance among influenza viruses is essential
- Currently, there is no evidence of on-going transmission of oseltamivir-resistant 2009 H1N1 virus strains worldwide

Antiviral Resistance Among Influenza Viruses

Summary of antiviral resistance among influenza viruses worldwide, October 2010*

	Influenza A Viruses		Influenza B Viruses Yamagata and Victoria lineages
Antiviral	**2009 H1N1**	**H3N2**	**B**
Adamantanes (Not recommended)	Resistant	Resistant	Resistant
Oseltamivir	Susceptible	Susceptible	Susceptible
Zanamivir	Susceptible	Susceptible	Susceptible

*Information on antiviral resistance is updated weekly and is available at www.cdc.gov/flu/weekly.
Rare instances of oseltamivir resistance among 2009 H1N1 viruses have been reported.
Over 99% of influenza viruses circulating since September 2009 have been sensitive to oseltamivir

Use of Antivirals

Treatment efficacy and effectiveness studies

- Oseltamivir or Zanamivir can reduce the duration of uncomplicated influenza A and B illness by approximately 1 to 1.5 days when administered within 48 hours of illness onset in randomized placebo-controlled clinical trials
- One observational study indicated that early oseltamivir treatment reduced the progression to CXR-confirmed pneumonia
- No published RCTs for antiviral treatment of hospitalized patients with severe influenza
- Observational studies of hospitalized patients with seasonal influenza (primarily elderly patients) or 2009 H1N1 (all ages, including pregnant women) indicate that early neuraminidase inhibitor treatment (primarily with oseltamivir) is associated with reduced morbidity and mortality
  - Treatment up to <5 days from illness onset is associated with reduced risk of ICU admission or death
- Limited data on effectiveness of zanamivir or oseltamivir treatment in preventing serious influenza-related complications (e.g., bacterial or viral pneumonia or exacerbation of chronic diseases)

Use of Antivirals

Treatment indications

- Benefits of antiviral treatment
  - Greatest if treatment is started as soon as possible after illness onset
  - Evidence for benefit is strongest in studies when treatment was started within 48 hours of illness onset
- However, antiviral treatment of any person with influenza who requires hospitalization is recommended as soon as possible, even if the patient presents more than 48 hours after illness onset

Use of Antivirals

Treatment indications (continued)

- During influenza season…
  - Consider influenza virus infection as the possible cause of any febrile illness requiring hospitalization during influenza season
  - Consider empiric antiviral therapy in patients with suspected influenza as clinically indicated; consider influenza testing if testing will influence treatment decisions, but be aware of limitations of influenza tests and how to interpret test results
  - Monitor local, state and national recommendations during the influenza season to determine the most appropriate treatment practices
  - Receive updates on antiviral resistance profiles of the circulating viruses
- Treatment decisions should be informed by knowledge of influenza activity in the community

Use of Antivirals

Treatment indications (continued)

- Empiric antiviral treatment is recommended
- Treatment initiation should not be delayed while awaiting specimen collection or influenza testing results
- Patients should continue to receive antiviral treatment regardless of negative initial test results until an alternative diagnosis can be established
- Clinicians who prefer not to treat empirically should:
  - Discuss signs and symptoms of worsening illness with patients
  - Arrange for follow up by telephone or in the clinic

Use of Antivirals

Treatment indications (continued)

- **Antiviral treatment is recommended as early as possible for any patient with confirmed of suspected influenza who:**
  - **Has severe, complicated, or progressive illness; or**
  - **Is hospitalized; or**
  - **Is at higher risk for influenza complications**
- 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.
  - Although all children <2 years are at risk for severe complications from influenza, the risk is highest among young infants <6 months old. Because many children with mild febrile respiratory illness may have other viral infections (e.g. RSV, rhinovirus, parainfluenza, metapneumovirus), knowledge about other respiratory viruses as well as influenza virus strains circulating in the community is important for treatment decisions

Use of Antivirals

Treatment indications (continued)

- Persons at higher risk for influenza complications who are recommended for antiviral treatment for confirmed or suspected influenza include the following:
  - Children younger than 2 years old (the risk is highest among <6 months old)
  - Adults 65 years of age and older;
  - Persons with the following conditions: chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), metabolic disorders (including diabetes mellitus), and 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];
  - Immunosuppression, including that caused by medications or by HIV infection;
  - Women who are pregnant or postpartum (within 2 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 equal to or greater than 40);
  - Residents of nursing homes and other chronic care facilities

Use of Antivirals

Treatment indications (continued)

- For outpatients, antiviral treatment with a neuraminidase inhibitor is recommended for all persons:
  - With confirmed or suspected influenza who are at a higher risk for influenza complications due to age or underlying medical conditions
- Antibacterial therapy plus antiviral treatment is recommended for patients with community-acquired pneumonia when influenza is also suspected
- Data on effectiveness of antiviral treatment of critically ill patients are very limited

Use of Antivirals

Treatment indications (continued)

- Previously healthy, non high-risk, symptomatic outpatients with confirmed or suspected uncomplicated influenza:
  - Antiviral treatment can be considered based upon clinical judgment if treatment can be initiated within 48 hours of illness onset
- These patients typically do not require treatment, but early empiric treatment might provide benefit, such as shortened duration of illness or reduced risk of clinical progression
- These patients are not likely to benefit from treatment if initiated more than 48 hours after illness onset
- Persons with influenza who are already beginning to recover do not need treatment

Use of Antivirals

Treatment Indications (continued)

Recommendations for the selection of antiviral treatment using laboratory test results and viral surveillance data, United States, 2010-11 season*

Rapid antigen, RT-PCR or other laboratory test	Preferred medication(s) †	Alternative (combination antiviral treatment)
Not done or negative, but clinical suspicion for influenza†	Oseltamivir or Zanamivir	None
Positive A or positive A+B§	Oseltamivir or Zanamivir	None
Positive 2009 influenza A(H1N1)	Oseltamivir or zanamivir	None
Positive A(H3N2), or B	Oseltamivir or zanamivir	None

* **Note that antiviral recommendations may change over time.** Influenza antiviral medications used for treatment are most beneficial when initiated within the first two days of illness. Clinicians should consult the package insert of each antiviral medication for specific dosing information, approved indications and ages, contraindications/warnings/precautions, and adverse effects.

†Viral surveillance data might help guide antiviral choices if oseltamivir resistance becomes more prevalent. Consult guidance from local or state public health laboratories or CDC for further information on currently circulating viruses. CDC viral surveillance data is updated weekly during the influenza season, and available at www.cdc.gov/flu/weekly.

§ Positive A+B indicates a rapid antigen test that cannot distinguish between influenza A and influenza B viruses.

Use of Antivirals

Treatment issues for patients hospitalized with confirmed or suspected influenza

- Treatment regiments 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
- No controlled data are available to evaluate the effectiveness of higher doses of antivirals to treat severe influenza illness
- Administering oseltamivir via gastric tube can provide systemic absorption in some critically ill patients
  - Gastric stasis or bleeding can make this route problematic
- Parenterally-administered neuraminidase inhibitors are not approved in the U.S.

Use of Antivirals

Treatment issues for patients hospitalized with confirmed or suspected influenza (continued)

- Intravenous zanamivir is available for compassionate use via EIND
- Clinical trials are needed to better understand optimal treatment approaches
- www.clinicaltrials.gov (eligibility and enrollment of patients in clinical trials of experimental intravenous antivirals (IV zanamivir, IV peramivir) or combination antiviral treatment

Use of Antivirals

Treatment issues for patients hospitalized with confirmed or suspected influenza (continued)

- Patients receiving antiviral medications who do not respond to treatment might have infection with an antiviral resistant influenza virus
- Infection control measures are especially important for patients who are immunocompromised to reduce the risk of transmission of oseltamivir-resistant influenza virus
- Oseltamivir resistance, sometimes within 1 week of treatment initiation, has been reported particularly among immunocompromised patients with 2009 pandemic influenza A (H1N1) virus infection who were receiving treatment with oseltamivir

Use of Antivirals

Chemoprophylaxis

- Chemoprophylaxis with antiviral medications is not a substitute for influenza vaccination when influenza vaccine is available
- The likelihood of compliance and adverse events should be considered when determining the timing and duration for administering influenza antiviral medications for chemoprophylaxis
- Failure to complete a course of oseltamivir for chemoprophylaxis due to gastrointestinal adverse events might lead to antiviral resistance if infection has occurred

Use of Antivirals

Post-exposure chemoprophylaxis

- Decisions regarding whether to administer antivirals for chemoprophylaxis should take into account:
  - The exposed person's risk for influenza complications
  - The type and duration of contact
  - Recommendations from local or public health authorities
    - In areas with limited antiviral medication availability, local public health authorities might recommend that antiviral medications be primarily directed at treatment and that antiviral chemoprophylaxis be used only in certain limited situations
  - Clinical judgment
- Generally, post-exposure chemoprophylaxis for individuals should only be used when antivirals can be started within 48 hours of the last exposure

Use of Antivirals

Post-exposure chemoprophylaxis (continued)

- An emphasis on early treatment is an alternative to chemoprophylaxis in managing some persons who have had a suspected exposure to a symptomatic person with influenza virus infection
  - Counsel them about early signs and symptoms of influenza
  - Advise them to immediately contact their health care provider for evaluation and possibly early treatment if clinical signs or symptoms of influenza develop
  - Counsel them about influenza antiviral medication side effects
  - Inform them that they remain susceptible to influenza virus infection after the antiviral medications are stopped
- Health care providers should use clinical judgment regarding situations where early recognition of illness and early antiviral treatment might be an appropriate alternative

Use of Antivirals

Post-exposure chemoprophylaxis (continued)

- Post-exposure chemoprophylaxis with neuraminidase inhibitors should generally be reserved for those who have had recent close contact with a person with symptomatic influenza
- Persons who can be considered for antiviral chemoprophylaxis include:
  - Family or other close contacts of suspected or confirmed case
    - Who are at higher risk of influenza complications , and
    - Who have not been vaccinated against the influenza virus strains circulating at the time of exposure
  - Residents of institutions during confirmed or suspected influenza outbreaks
  - Unvaccinated health care workers
    - Who have occupational exposures, and
    - Who did not have adequate personal protective equipment at the time of exposure

Use of Antivirals

Post-exposure chemoprophylaxis (continued)

- Either oseltamivir or zanamivir is recommended for antiviral chemoprophylaxis of 2009 H1N1, influenza A (H3N2), or influenza B influenza virus infection
- Persons who receive an antiviral medication for chemoprophylaxis might still acquire influenza virus infection and be potentially able to transmit infection, even if clinical illness is prevented
- Antiviral chemoprophylaxis is approximately 70-80% effective in preventing illness, but not necessarily influenza virus infection when exposure to drug sensitive virus occurs

Use of Antivirals

Post-exposure chemoprophylaxis (continued)

- Patients given post-exposure antiviral chemoprophylaxis should:
  - Be informed that the chemoprophylaxis lowers but does not eliminate the risk of influenza
  - Be informed that susceptibility to influenza returns once the antiviral medication is stopped
  - Be encouraged to seek medical evaluation as soon as they develop a febrile respiratory illness that might indicate influenza (infection can still occur, might be a resistant virus)

- Post-exposure chemoprophylaxis is typically given up to 10 days after last known exposure to a close contact known to have influenza

Use of Antivirals

Pre-exposure chemoprophylaxis

- Pre-exposure chemoprophylaxis should only be used for persons who are:
  - At very high risk of influenza-related complications, and
  - Cannot otherwise be protected during times when there is a high risk for exposure
- Use should be in accordance with current recommendations from CDC or local public health authorities
- When used, pre-exposure chemoprophylaxis must be given for the duration of time when exposure might occur
- To be maximally effective, the drug must be taken each day for the duration of influenza activity in the community
- The adverse events associated with long term use are uncertain, and prolonged use of antivirals might select for resistance to antiviral medications

Use of Antivirals

Pre-exposure chemoprophylaxis (continued)

- In community studies of healthy adults given antiviral medications during times of influenza virus transmission, both oseltamivir and zanamivir had similar efficacy in preventing febrile, lab-confirmed influenza illness
- Studies have also demonstrated efficacy for prevention of influenza among patients in institutional settings
- Date are limited on the efficacy and effectiveness of antiviral agents in preventing influenza among severely immunocompromised persons

Use of Antivirals

Considerations for use if oseltamivir-resistant influenza virus strains are circulating

- Since 2009, 99% of circulating influenza A and B viruses have been susceptible to oseltamivir (i.e., seasonal influenza A (H1N1) viruses have not been detected in the U.S. since 2009)
- CDC provides weekly updates on virus surveillance at the national level (http://www.cdc.gov/flu/weekly/fluactivitysurv.htm)
- If oseltamivir resistant viruses are not circulating, antiviral treatment for influenza should consist of either oseltamivir or zanamivir
- Continued changes in antiviral resistance are likely among influenza viruses; clinicians should remain attentive to updates in antiviral treatment guidance

Use of Antivirals

Control of influenza outbreaks in institutions

- Antiviral drug treatment /chemoprophylaxis are key to outbreak control in institutions with patients at higher risk for influenza complications
- Neuraminidase inhibitors have been used to successfully control outbreaks when combined with other infection control measures, and influenza vaccination
- Zanamivir should be used when persons require chemoprophylaxis due to exposure to influenza virus strains that are suspected of being oseltamivir-resistant
- Obtain respiratory specimens from ill persons for influenza typing, influenza A virus subtyping (RT-PCR) or viral culture (for antigenic characterization and to assess antiviral resistance) and provide data on the outbreak etiology
- If chemoprophylaxis is indicated, start neuraminidase inhibitors as early as possible
  - Helpful to have preapproved orders from physicians , plans to obtain orders for antiviral medications on short notice

Use of Antivirals

Control of influenza outbreaks in institutions (continued)

- Administer chemoprophylaxis to all eligible residents, regardless of influenza vaccination status
  - Chemoprophylaxis should last for a minimum of 2 weeks
  - If new cases continue to occur, continue until approx.10 days after illness onset in the last patient
- Also offer to unvaccinated staff who care for high-risk persons
- Measures should be taken to reduce contact between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis

Use of Antivirals

Control of influenza outbreaks in institutions (continued)

- Other outbreak-control measures :
  - institute droplet and contact precautions , establish cohorts of patients with confirmed or suspected influenza
  - re-offer influenza vaccination (if available) to unvaccinated staff , patients
  - restrict staff movement between wards or buildings
  - restrict contact between ill staff or visitors and patients

Use of Antivirals

Dosage

Table 1: Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2010-11 Season—United States

Antiviral agent		Age group (yrs)				
		1*-6	7-9	10-12	13-64	65 and older
Zanamivir	Treatment, influenza A and B	N/A†	10 mg (2 inhalations) twice daily	10 mg (2 inhalations) twice daily	10 mg (2 inhalations) twice daily	10 mg (2 inhalations) twice daily
	Chemoprophylaxis, influenza A and B	**Ages 1-4** N/A	**Ages 5-9** 10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily	10 mg (2 inhalations) once daily
Oseltamivir	Treatment†, influenza A and B	Dose varies by child's weight§	Dose varies by child's weight§	Dose varies by child's weight§ >40 kg = adult dose	75 mg twice daily	75 mg twice daily
	Chemoprophylaxis, influenza A and B	Dose varies by child's weight¶	Dose varies by child's weight¶	Dose varies by child's weight¶ >40 kg = adult dose	75 mg once daily	75 mg once daily
Duration of Treatment	**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.				
	Chemoprophylaxis	Recommended duration is 10 days when given after a household exposure, and 7 days after last known exposure in other situations For control of outbreaks in long-term care facilities and hospitals, CDC recommends antiviral chemoprophylaxis for a minimum of two weeks, and up to one week after the last known case was identified.				

Use of Antivirals

Dosage

NOTE: Zanamivir is manufactured by GlaxoSmithKline (Relenza — inhaled powder). Zanamivir is approved for treatment of persons aged 7 years and older and approved for chemoprophylaxis of persons aged 5 years and older. Zanamivir is administered through oral inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of the correct use of the device. Zanamivir is not recommended for those persons with underlying airway disease. Oseltamivir is manufactured by Roche Pharmaceuticals (Tamiflu® — tablet) Oseltamivir is approved for treatment or chemoprophylaxis of persons aged 1 year and older. No antiviral medications are approved for treatment or chemoprophylaxis of influenza among children younger than 1 year of age. This information is based on data published by the Food and Drug Administration (FDA).

* See Table 4 for information about use of oseltamivir for infants aged <1 year.

† A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance less than 30 mL/min.

§ The treatment dosing recommendation for oseltamivir for children aged >1 year who weigh 15 kg or less is 30 mg twice a day. For children who weigh more than 15 kg and up to 23 kg, the dose is 45 mg twice a day. For children who weigh more than 23 kg and up to 40 kg, the dose is 60 mg twice a day. For children who weigh more than 40 kg, the dose is 75 mg twice a day.

¶ The chemoprophylaxis dosing oseltamivir recommendation for children aged >1 year who weigh 15 kg or less is 30 mg once a day. For who weigh more than 15 kg and up to 23 kg, the dose is 45 mg once a day. For children who weigh more than 23 kg and up to 40 kg, the dose is 60 mg once a day. For children who weigh more than 40 kg, the dose is 75 mg once a day.

Use of Antivirals

Dosage (continued)

Dosing recommendations for treatment or chemoprophylaxis of children younger than 1 year using oseltamivir.*

Age	Recommended treatment dose for 5 days†	Recommended chemoprophylaxis dose for 10 days†
<3 months	3 mg/kg/dose twice daily	Not recommended unless situation judged critical due to limited data on use in this age group
3-<12 months	3 mg/kg/dose twice daily	3 mg/kg/dose once daily

*This Emergency Use Authorization (EUA) was issued by the Food and Drug Administration on April 28, 2009, and has expired. This EUA allowed use of oseltamivir for treatment or chemoprophylaxis of 2009 pandemic influenza A (H1N1) virus infection in infants aged <1 year during the pandemic. Currently circulating 2009 H1N1, seasonal influenza A(H3N2) and B viruses have similar sensitivity to oseltamivir.

†Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants may have slower clearance of oseltamivir due to immature renal function, and doses recommended for full term infants may lead to very high drug concentrations in this age group. Very limited data from a cohort of premature infants demonstrated that oseltamivir concentrations among premature infants given 1 mg/kg twice daily higher were similar to those observed with the recommended treatment dose in term infants (3 mg/kg twice daily). Observed drug concentrations were highly variable among premature infants. These data are insufficient to recommend a specific dose of oseltamivir for premature infants.

Questions?

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
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Centers for Disease Control and Prevention, Atlanta GA

Continuing Education Credit/Contact Hours for COCA Conference Calls

Continuing Education guidelines require that the attendance of all who participate in COCA Conference Calls be properly documented. All Continuing Education credits/contact hours (CME, CNE, CEU, CECH, and ACPE) for COCA Conference Calls are issued online through the CDC Training & Continuing Education Online system http://www2a.cdc.gov/TCEOnline/.

Those who participate in the COCA Conference Calls and who wish to receive CE credit/contact hours and will complete the online evaluation by **Dec 30 2010** will use the course code **EC1648**. Those who wish to receive CE credits/contact hours and will complete the online evaluation between **Dec 31, 2010** and **Dec 30, 2011** will use course code **WD1648**. CE certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Thank you for joining!
Please email us questions at coca@cdc.gov