

## Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season

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### Objective

To provide updated guidance on the use of antiviral agents for treatment and chemoprophylaxis of influenza including 2009 H1N1 influenza infection and seasonal influenza, and assist clinicians in prioritizing use of antiviral medications for treatment or chemoprophylaxis for patients at higher risk for influenza-related complications. Additional revisions to these recommendations should be expected as the epidemiology and clinical presentation of 2009 H1N1 influenza is better understood. This guidance can be adapted according to local epidemiologic data, antiviral susceptibility patterns, and antiviral supply considerations. Clinical judgment is always an important part of treatment decisions.

### Summary

- Treatment with oseltamivir or zanamivir is recommended for all persons with suspected or confirmed influenza requiring hospitalization.
- Treatment with oseltamivir or zanamivir generally is recommended for persons with suspected or confirmed influenza who are at higher risk for complications (children younger than 5 years old, adults 65 years and older, pregnant women, persons with certain chronic medical or immunosuppressive conditions, and persons younger than 19 years of age who are receiving long-term aspirin therapy).
- Persons who are not at higher risk for complications or do not have severe influenza requiring hospitalization generally do not require antiviral medications for treatment or prophylaxis. However, any suspected influenza patient presenting with warning symptoms (e.g., dyspnea) or signs (e.g., tachypnea, unexplained oxygen desaturation) for lower respiratory tract illness should promptly receive empiric antiviral therapy.
- Clinical judgment is an important factor in antiviral treatment decisions for all patients presenting for medical care who have illnesses consistent with influenza.
- Treatment should be initiated as early as possible because studies show that treatment initiated early (i.e., within 48 hours of illness onset) is more likely to provide benefit.
- Treatment should not wait for laboratory confirmation of influenza because laboratory testing can delay treatment and because a negative rapid test for influenza does not rule out influenza. The sensitivity of rapid tests can range from 10 % to 70%. Information on the use of rapid influenza diagnostic tests (RIDTs) can be found at [http://www.cdc.gov/h1n1flu/guidance/rapid\\_testing.htm](http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm).

- Testing for 2009 H1N1 influenza infection with real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) should be prioritized for persons with suspected or confirmed influenza requiring hospitalization and based on guidelines from local and state health departments.
- Groups at higher risk for 2009 H1N1 influenza complications are similar to those at higher risk for seasonal influenza complications.
- Actions that should be taken to reduce delays in treatment initiation include:
  - Informing persons at higher risk for influenza complications of signs and symptoms of influenza and need for early treatment after onset of symptoms of influenza (i.e., fever, respiratory symptoms);
  - Ensuring rapid access to telephone consultation and clinical evaluation for these patients as well as patients who report severe illness;
  - Considering empiric treatment of patients at higher risk for influenza complications based on telephone contact if hospitalization is not indicated and if this will substantially reduce delay before treatment is initiated.
- In selected circumstances, providers might also choose to provide selected patients at higher risk for influenza-related complications (e.g., patients with neuromuscular disease) with prescriptions that can be filled at the onset of symptoms after telephone consultation with the provider.
- Antiviral chemoprophylaxis generally should be reserved for persons at higher risk for influenza-related complications who have had contact with someone likely to have been infected with influenza.
- Based on global experience to date, 2009 H1N1 influenza viruses likely will be the most common influenza viruses among those circulating in the coming season, particularly those causing influenza among younger age groups. Circulation of seasonal influenza viruses during the 2009-10 season is also expected. Influenza seasons are unpredictable, however, and the timing and intensity of seasonal influenza virus activity versus 2009 H1N1 circulation cannot be predicted in advance.
- Persons with suspected 2009 H1N1 influenza or seasonal influenza who present with an uncomplicated febrile illness typically do not require treatment. However, some groups appear to be at higher risk for influenza-related complications.
- Currently circulating 2009 H1N1 viruses are susceptible to oseltamivir and zanamivir, but resistant to amantadine and rimantadine; however, antiviral treatment regimens might change according to new antiviral resistance or viral surveillance information.
- Information on the dose and dosing schedule for oseltamivir and zanamivir is provided in this document. An April 2009 Emergency Use Authorization

authorizes the emergency use of oseltamivir in children younger than 1 year old (<http://www.cdc.gov/h1n1flu/eua/>), subject to the terms and conditions of the EUA

## **Background**

As of August, 2009, more than 98% of circulating influenza viruses in the United States were 2009 H1N1 influenza (previously referred to as novel influenza A (H1N1)). Among people who become infected with 2009 H1N1, certain groups appear to be at increased risk of complications and may benefit most from early treatment with antiviral medications. Approximately 70% of persons hospitalized from 2009 H1N1 influenza have had a recognized high risk condition (approximately 60% of children and approximately 80% among adults). These high risk conditions are the same conditions that increase the risk of complications from seasonal influenza infection.

- Children younger than 5 years old. However, the risk for severe complications from seasonal influenza is highest among children younger than 2 years old.
- Adults 65 years of age or older
- Pregnant women
- Persons with the following conditions:
  - Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), neurologic, neuromuscular, or metabolic disorders (including diabetes mellitus);
  - Immunosuppression, including that caused by medications or by HIV;
  - Persons younger than 19 years of age who are receiving long-term aspirin therapy, because of an increased risk for Reye syndrome.

Among children, rates of influenza hospitalization from 2009 H1N1 have varied by age group with the highest rates of hospitalization in children younger than 2 years of age. Updated information on hospitalization rates by age group can be found at [www.cdc.gov/flu/weekly](http://www.cdc.gov/flu/weekly).

People 65 and older are at lower risk of infection from 2009 H1N1 compared to younger age groups. However, as with seasonal influenza, people 65 or older who develop 2009 H1N1 influenza infection are at increased risk of influenza-related complications compared to younger adults.

Preliminary studies suggest that people who are morbidly obese (body mass index equal to or greater than 40) and perhaps people who are obese (body mass index 30 to 39) may be at increased risk of hospitalization and death due to 2009 H1N1 influenza infection. Additional studies to determine the risk of morbid obesity and /or obesity for these complications of 2009 H1N1 virus infection are underway. Patients with morbid obesity, and perhaps obesity, often have underlying conditions that put them at increased risk for complications due to 2009 H1N1 influenza infection, such as diabetes, asthma, chronic

respiratory illness or liver disease. Patients with obesity or morbid obesity should be carefully evaluated for the presence of underlying medical conditions that are known to increase the risk for influenza complications, and receive empiric treatment when these conditions are present, or if signs of lower respiratory tract infection are present.

Transmission of 2009 H1N1 influenza is being studied as part of the ongoing epidemiologic investigation, but data available indicate that this virus appears to be transmitted in ways similar to other influenza viruses. All respiratory secretions and bodily fluids (including diarrheal stool) of 2009 H1N1 cases should be considered potentially infectious.

*Close contact, for the purposes of this document, is defined as having cared for or lived with a person who is a confirmed, probable, or suspected case of influenza, or having been in a setting where there was a high likelihood of contact with respiratory droplets and/or body fluids of such a person. Examples of close contact include sharing eating or drinking utensils, physical examination, or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person or sitting across from a symptomatic patient in a waiting room or office.*

### ***Special Considerations for Children***

*Aspirin or aspirin-containing products (e.g. bismuth subsalicylate – Pepto Bismol) should not be administered to any confirmed or suspected ill case of influenza aged 18 years old and younger due to the risk of Reye syndrome. For relief of fever, other anti-pyretic medications such as acetaminophen or non-steroidal anti-inflammatory drugs are recommended.*

*Children younger than 4 years of age should not be given over-the-counter cold medications without first speaking with a healthcare provider.*

## **Antiviral Treatment**

Recommendations for use of antiviral medications may change as data on antiviral effectiveness, clinical spectrum of illness, adverse events from antiviral use, or resistance among circulating viruses become available. As of August 2009, more than 98% of circulating influenza viruses were 2009 H1N1 viruses susceptible to both oseltamivir and zanamivir. These treatment guidelines therefore focus on use of antiviral medications effective against 2009 H1N1 viruses. For antiviral treatment of 2009 H1N1 virus infection, either oseltamivir or zanamivir are recommended ([Table 1](#)).

Clinical judgment is an important factor in treatment decisions. Most patients who have had 2009 H1N1 virus infection have had a self-limited respiratory illness similar to typical seasonal influenza. Persons with suspected 2009 H1N1 influenza or seasonal influenza who present with an uncomplicated febrile illness generally do not require treatment. However, some groups appear to be at increased risk of influenza-related complications. Local public health authorities might provide additional guidance about prioritizing treatment within groups at higher risk for severe infection.

1. Treatment is recommended for all hospitalized patients with confirmed, probable or suspected 2009 H1N1 or seasonal influenza.
2. Treatment generally is recommended for patients who are at higher risk for influenza-related complications (see above).
3. Treatment should be initiated empirically when the decision is made to treat patients who have illnesses that are clinically compatible with influenza. Treatment should not await laboratory confirmation because laboratory testing can sometimes delay treatment and because a negative rapid test does not rule out influenza. (See “Evaluation of Rapid Influenza Diagnostic Tests for Detection of Novel Influenza A (H1N1) Virus --- United States, 2009” for more information about the sensitivity of rapid tests.)

These recommendations should be used together with clinical judgment in making treatment decisions for both patients who are at higher risk for influenza-related complications and patients who are not at higher risk. When evaluating previously healthy children with possible influenza, clinicians should be aware that, similar to seasonal influenza, the risk for severe disease is likely to be highest among infants and younger children. Once the decision to administer antiviral treatment is made by the health care provider, treatment with zanamivir or oseltamivir should be initiated as soon as possible after the onset of symptoms.

Evidence for benefits from antiviral treatment in studies of uncomplicated seasonal influenza is strongest when treatment is started within 48 hours of illness onset. Initiating treatment as soon as possible after illness onset is also thought likely to reduce the risk of severe outcomes including severe illness or death. However, some studies of hospitalized patients with seasonal influenza treated with oseltamivir have suggested benefit, including reductions in mortality or duration of hospitalization, even for patients whose treatment was started more than 48 hours after illness onset. The recommended duration of treatment is five days. Hospitalized patients with severe infections (such as those with prolonged infection or who require intensive unit care admission) might require longer treatment courses. Antiviral doses recommended for treatment of 2009 H1N1 influenza virus infection in adults or children 1 year of age or older are the same as those recommended for seasonal influenza (Table 1). Some experts have advocated use of increased (doubled) doses of oseltamivir for some severely ill patients, although there are no published data demonstrating that higher doses are more effective. Oseltamivir use for children younger than 1 year old was recently authorized by the U.S. Food and Drug Administration (FDA) under an Emergency Use Authorization (EUA). These EUA provisions apply only when the product is provided in accordance with the local public health authority's response plans. Dosing for children younger than 1 year old is age-based in the EUA guidance. However, some experts who are currently conducting studies on oseltamivir use in this age group prefer weight based dosing for this age group, particularly for premature or underweight infants. (Table 2) (See Emergency Use Authorization of Tamiflu (oseltamivir) available at <http://www.cdc.gov/h1n1flu/eua/>).

Persons at higher risk for complications from influenza or who have already developed severe illness should be treated as quickly as possible after signs or symptoms develop. To reduce delays in starting treatment, health care providers should:

- 1) Provide information for patients at higher risk for influenza complications about signs and symptoms of influenza and need for early treatment after symptom onset when ill with influenza;
- 2) Ensure rapid access to telephone consultation and clinical evaluation for these patients as well as patients who report severe illness;
- 3) Consider empiric treatment of patients at higher risk for influenza complications based on telephone contact if hospitalization is not indicated and if this will substantially reduce delay before treatment is initiated;
- 4) Request that patients at higher risk for influenza complications contact the provider if signs or symptoms of influenza develop, obtain the medication as quickly as possible and initiate treatment. In selected circumstances, providers may consider giving a prescription for an influenza antiviral to selected patients who are higher risk for influenza complications. When considering providing a prescription to patients for future use, providers might take into account patient reliability, ability to understand the information about symptoms of influenza, and access to a pharmacy. Providers might prefer to provide a prescription that requires a telephone consultation with the provider before it can be filled.
- 5) Counsel patients about influenza antiviral benefits and adverse effects, the potential for continued susceptibility to influenza virus infection after treatment is completed (because of other circulating influenza viruses or if illness was due to another cause), and the need to again seek early access to health care consultation if symptoms recur.

State prescribing and dispensing laws and requirements might differ. Clinicians should take applicable state prescribing and dispensing laws and requirements into account in considering these recommendations.

Patients receiving treatment should be advised that they remain potentially infectious to others while on treatment. Despite treatment with antiviral agents, including treatment with the neuraminidase inhibitors, patients may continue to shed influenza virus for up to four or more days after beginning therapy. Therefore, patients should continue good hand washing and respiratory hygiene practices during the entire period on therapy to prevent the transmission of virus to close contacts. Information about homecare of ill persons for providers and patients is available at [http://www.cdc.gov/h1n1flu/guidance\\_homecare.htm](http://www.cdc.gov/h1n1flu/guidance_homecare.htm) and [http://www.cdc.gov/h1n1flu/guidance\\_homecare\\_directions.htm](http://www.cdc.gov/h1n1flu/guidance_homecare_directions.htm)

### **Treatment of influenza when oseltamivir-resistant viruses are circulating**

Oseltamivir resistance is common among seasonal influenza A (H1N1) viruses. These viruses typically remain susceptible to rimantadine and amantadine. However, since April 2009, very few seasonal H1N1 viruses have circulated in the United States. Therefore, treatment, when indicated, with either oseltamivir or zanamivir is appropriate. However, if viral surveillance data indicate that oseltamivir-resistant seasonal H1N1 viruses have

become more common or are associated with identified community outbreaks, zanamivir or a combination of oseltamivir and rimantadine or amantadine should be considered for use as empiric treatment for patients who might have oseltamivir-resistant seasonal human influenza A (H1N1) virus infection. National surveillance data on influenza viruses circulating in the United States is available at [www.cdc.gov/flu](http://www.cdc.gov/flu) and is updated weekly. State and local health departments are also a source of viral surveillance data in some areas. Guidance on empiric treatment recommendations when multiple influenza strains are circulating is available at <http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00279>.

### **Antiviral Chemoprophylaxis**

The infectious period for persons infected with the 2009 H1N1 virus appears to be similar to that observed in studies of seasonal influenza. Infected persons may shed influenza virus, and potentially be infectious to others, beginning one day before they develop symptoms to up to 7 days after they become ill. Children, especially younger children, can shed influenza virus for longer periods. However, for this guidance, the *infectious period* for influenza is defined as one day before until 24 hours after fever ends.

- **Post exposure antiviral chemoprophylaxis with either oseltamivir or zanamivir can be considered for the following:**
  - Persons who are at higher risk for complications of influenza and are a close contact of a person with confirmed, probable, or suspected 2009 H1N1 or seasonal influenza during that person's infectious period.
  - Health care personnel, public health workers, or first responders who have had a recognized, unprotected close contact exposure to a person with confirmed, probable, or suspected 2009 H1N1 or seasonal influenza during that person's infectious period. Information on appropriate personal protective equipment is available at: [Infection Control for Patients in a Healthcare Setting](#) and might be updated frequently as additional information on transmission becomes available.
- Antiviral agents should not be used for post exposure chemoprophylaxis in healthy children or adults based on potential exposures in the community, school, camp or other settings.
- Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person.
- Chemoprophylaxis is not indicated when contact occurred before or after, but not during, the ill person's infectious period as defined above.

Patients given post-exposure chemoprophylaxis should be informed that the chemoprophylaxis lowers but does not eliminate the risk of influenza and that protection stops when the medication course is stopped. Patients receiving chemoprophylaxis should be encouraged to seek medical evaluation as soon as they develop a febrile respiratory

illness that might indicate influenza. For antiviral chemoprophylaxis of 2009 H1N1 influenza virus infection, either oseltamivir or zanamivir is recommended (Table 1). Duration of post-exposure chemoprophylaxis is 10 days after the last known exposure to 2009 H1N1 influenza.

Oseltamivir was authorized for use for chemoprophylaxis under the EUA for children younger than 1 year of age, subject to the terms and conditions of the EUA. (See Treatment and Chemoprophylaxis for Children Younger than 1 Year of Age, below.) Age-based dosing recommendations are provided in the fact sheets included with the EUA letter of authorization, however weight-based dosing is an alternative preferred by some experts who are currently conducting studies of oseltamivir use in this age group.

**An emphasis on early treatment is an alternative to chemoprophylaxis after a suspected exposure for some persons.** Persons with risk factors for influenza complications who are household or close contacts of confirmed or suspected cases, and health care personnel who have occupational exposures, can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their health care provider for evaluation and possible early treatment if clinical signs or symptoms develop. Health care providers should use clinical judgment regarding situations where early recognition of illness and treatment might be an appropriate alternative. In some exposure circumstances (e.g., person exposed is at higher risk for complications), health care providers might choose to give the exposed patient a prescription for an influenza antiviral. Providers can request that the patient contact the provider if signs or symptoms of influenza develop, obtain antiviral medications as quickly as possible, and initiate treatment. These patients should also be counseled about influenza antiviral medication side effects, and informed that they remain susceptible to influenza after treatment is completed.

Persons at ongoing occupational risk for exposure (e.g., health care personnel, public health workers, or first responders who are working in communities with influenza outbreaks) should carefully follow guidelines for appropriate personal protective equipment. Appropriate administrative controls (e.g. having health care personnel stay home from work when ill, and triaging for identification of potentially infectious patients) and personal protective equipment should be used to reduce the need for post-exposure chemoprophylaxis among health care workers.

### **Antiviral Resistance**

2009 H1N1 influenza viruses are susceptible to the neuraminidase inhibitor antiviral medications, oseltamivir and zanamivir, but are resistant to the adamantane antiviral medications, amantadine and rimantadine. This susceptibility pattern is the same as that observed among seasonal influenza A (H3N2) and B viruses in recent years. Oseltamivir resistance appears to be rare at this time. However, oseltamivir-resistant 2009 H1N1 viruses have been identified, typically among persons who develop illness while receiving oseltamivir for chemoprophylaxis or immunocompromised patients with influenza who are being treated. **These findings underscore the importance of careful and limited use of antiviral medications for chemoprophylaxis and the need for persons taking antiviral medications to continue to follow recommendations for**

**hand and respiratory hygiene to prevent the spread of antiviral resistant viruses.** Additional information on oseltamivir resistance among 2009 H1N1 viruses is available at <http://www.cdc.gov/h1n1flu/HAN/070909.htm>. Monitoring for antiviral resistance is ongoing and clinicians and state health departments should continue to follow state and national guidance for submission and testing of clinical specimens from persons with suspected 2009 H1N1 virus infection, particularly from those who develop influenza while taking chemoprophylaxis or who have prolonged viral shedding while on treatment.

### **Antiviral Use for Control of 2009 H1N1 Influenza Outbreaks**

Use of antiviral drugs for treatment and chemoprophylaxis of influenza has been a cornerstone for the control of seasonal influenza outbreaks in nursing homes and other long-term care facilities that house large numbers of patients at higher risk for influenza complications. (See MMWR: Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008). At this time, no outbreaks of 2009 H1N1 have been reported in such settings. This may be the result of some level of immunity among persons 65 years and older and/or possibly fewer exposures of such persons to 2009 H1N1 thus far. However, if such outbreaks were to occur, it is recommended that ill patients be treated with oseltamivir or zanamivir and that chemoprophylaxis with either oseltamivir or zanamivir be started as early as possible to reduce the spread of the virus as is recommended for seasonal influenza outbreaks in such settings. Additional guidance for infection control measures in long-term care facilities can be found at: Using Antiviral Medications to Control Influenza Outbreaks in Institutions.

In addition to use in nursing homes, antiviral chemoprophylaxis also can be considered for controlling influenza outbreaks in other closed or semi-closed settings (e.g., correctional facilities, or other settings in which persons live in close proximity) where persons at higher risk for influenza complications are housed. For more information about influenza outbreaks in facilities see:

- 1) Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009 (Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5808a1.htm>)
- 2) Seasonal Influenza in Adults and Children—Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America (available at: <http://www.journals.uchicago.edu/doi/pdf/10.1086/598513>).
- 3) Interim Guidance for Correctional and Detention Facilities on Novel Influenza A (H1N1) Virus (Available at: [http://www.cdc.gov/h1n1flu/guidance/correctional\\_facilities.htm](http://www.cdc.gov/h1n1flu/guidance/correctional_facilities.htm))
- 4) Interim Guidance for Homeless and Emergency Shelters on the Novel Influenza A (H1N1) Virus (Available at: <http://www.cdc.gov/h1n1flu/guidance/homeless.htm>)

Outbreaks in schools, camps, workplaces and other group settings should not be managed by providing chemoprophylaxis to all persons potentially exposed to influenza viruses. The healthy populations typically present in these settings should be educated about the signs and symptoms of influenza, and urged to consult their health care provider if severe illness develops. Post-exposure chemoprophylaxis can be considered for those who meet the above criteria for exposure and who have a medical condition that confers a higher risk for influenza complications. An emphasis on early evaluation and treatment, as described above, is an alternative. Persons in these settings also should be educated about hygiene and infection control measures that can reduce transmission of influenza viruses.

Table 1. Antiviral medication dosing recommendations for treatment or chemoprophylaxis of 2009 H1N1 infection.

(Table extracted from [IDSA guidelines for seasonal influenza.](#))

Agent, group		Treatment (5 days)	Chemoprophylaxis (10 days)
<b>Oseltamivir</b>			
<b>Adults</b>		75-mg capsule twice per day	75-mg capsule once per day
<b>Children ≥ 12 months</b>	15 kg or less	60 mg per day divided into 2 doses	30 mg once per day
	16-23 kg	90 mg per day divided into 2 doses	45 mg once per day
	24-40 kg	120 mg per day divided into 2 doses	60 mg once per day
	more than 40 kg	150 mg per day divided into 2 doses	75 mg once per day
<b>Zanamivir</b>			
<b>Adults</b>		Two 5-mg inhalations (10 mg total) twice per day	Two 5-mg inhalations (10 mg total) once per day
<b>Children</b>		Two 5-mg inhalations (10 mg total) twice per day (age, 7 years or older)	Two 5-mg inhalations (10 mg total) once per day (age, 5 years or older)

### **Treatment and Chemoprophylaxis for Children younger than 1 Year of Age**

Children younger than 1 year of age are at higher risk for influenza-related complications and have a higher rate of hospitalization compared to older children. Oseltamivir is not approved for use in children younger than 1 year of age. However, limited safety data on oseltamivir treatment of seasonal influenza in children younger than 1 year of age suggest that severe adverse events are rare. Oseltamivir is authorized for emergency use in

children younger than 1 year of age under an EUA issued by FDA, subject to the terms and conditions of the EUA.

Because infants experience high rates of morbidity and mortality from influenza, infants with 2009 H1N1 influenza virus infections may benefit from treatment using oseltamivir. (Table 2 and Emergency Use Authorization of Tamiflu (oseltamivir)).

Table 2. Dosing recommendations for antiviral treatment or chemoprophylaxis of children younger than 1 year using oseltamivir.

Age	Recommended treatment dose for 5 days	Recommended prophylaxis dose for 10 days
Younger than 3 months	12 mg twice daily	Not recommended unless situation judged critical due to limited data on use in this age group
3-5 months	20 mg twice daily	20 mg once daily
6-11 months	25 mg twice daily	25 mg once daily

Some experts prefer weight-based dosing for children aged younger than 1 year, particularly for very young or premature infants based on preliminary data from a National Institutes of Health- funded Collaborative Antiviral Study Group (CASG). When using weight-based dosing for infants aged younger than 1 year for treatment, those 9 months or older should receive 3.5 mg/kg/dose BID, and those aged younger than 9 months should receive 3.0 mg/kg/dose BID. When using weight-based dosing for infants aged younger than 1 year for chemoprophylaxis, those 9 months or older should receive 3.5 mg/kg/dose QD, and those aged younger than 9 months should receive 3.0 mg/kg/dose QD (Source: D Kimberlin et al. Oseltamivir (OST) and OST Carboxylate (CBX) Pharmacokinetics (PK) in Infants: Interim Results from a Multicenter Trial. Abstract accepted to Infectious Diseases Society of America meeting, October 2009). Health care providers should be aware of the lack of data on safety and dosing when considering oseltamivir use in a seriously ill young infant with confirmed 2009 H1N1 influenza virus infection or who has been exposed to a confirmed 2009 H1N1 influenza case, and carefully monitor infants for adverse events when oseltamivir is used. Additional information on oseltamivir for this age group can be found at: <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM153547.pdf>

### **Pregnant Women**

Pregnant women are known to be at higher risk for complications from infection with seasonal influenza viruses, and severe disease among pregnant women was reported during past pandemics. Hospitalizations and deaths have been reported among pregnant women with 2009 H1N1 influenza virus infection, and one study estimated that the risk

for hospitalization for 2009 H1N1 influenza was four times higher for pregnant women than for the general population. While oseltamivir and zanamivir are "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications for pregnant women, the available risk-benefit data indicate pregnant women with suspected or confirmed influenza should receive prompt antiviral therapy. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use. Because of its systemic activity, oseltamivir is preferred for treatment of pregnant women. The drug of choice for chemoprophylaxis is less clear. Zanamivir may be preferable because of its limited systemic absorption; however, respiratory complications that may be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems.

### **Adverse Events and Contraindications**

For further information about influenza and antiviral medications, including contraindications and adverse effects, please see the following:

- Antiviral Agents for Seasonal Influenza: Side Effects and Adverse Reactions.  
<http://www.cdc.gov/flu/professionals/antivirals/side-effects.htm>
- Harper SA, Bradley JS, Englund JA, et al. Infectious Diseases Society of America Guidelines. Seasonal Influenza in Adults and Children—Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America.  
<http://www.idsociety.org/content.aspx?id=9202#flu>
- Jamieson DJ, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet* 2009;374:451-8.
- CDC. Intensive-Care Patients With Severe Novel Influenza A (H1N1) Virus Infection --- Michigan, June 2009. 2009;58:749-52. Available at:  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5827a4.htm>
- Rasmussen SA. Pandemic Influenza and Pregnant Women: Summary of a Meeting of Experts. *Am J Public Health* 2009 (epub ahead of print).

Adverse events from influenza antiviral medications should be reported through the U.S. FDA Medwatch website.

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