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

October 16, 2009 4:00 PM ET

These recommendations have been updated to provide additional guidance for clinicians in prescribing antiviral medications for treatment and prevention of influenza during the 2009-2010 season. In general, the priority use of antiviral medications during this season continues to be in people who are hospitalized with influenza and those at increased risk of influenza-related complications as outlined in the recommendations last updated on September 22, 2009. This document has been updated to:

1. Clarify treatment and chemoprophylaxis considerations for persons vaccinated with the 2009 H1N1 and seasonal influenza vaccines.
2. Include women up to 2 weeks postpartum at higher risk for complications from 2009 H1N1 influenza.
3. Provide additional oseltamivir dosing instructions for children younger than 1 year of age.
4. Review adverse events and contraindications associated with oseltamivir and zanamivir.

This document should be considered interim, and will be updated as needed.

Summary

- Influenza antiviral medications can reduce the severity and duration of influenza illness and can reduce the risk of influenza-related complications, including severe illness and death.
- Most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment or prophylaxis. However, persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age.
- Treatment with oseltamivir or zanamivir is recommended for all persons with suspected or confirmed influenza requiring hospitalization.
- Early empiric treatment with oseltamivir or zanamivir should be considered for persons with suspected or confirmed influenza who are at higher risk for complications including:
 - Children younger than 2 years old;
 - Persons aged 65 years or older;
 - Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss);
 - Persons of any age with certain chronic medical or immunosuppressive conditions (see page 3); and,

- Persons younger than 19 years of age who are receiving long-term aspirin therapy.
- Children 2 year to 4 years old are more likely to require hospitalization or urgent medical evaluation for influenza compared with older children and adults, although the risk is much lower than for children younger than 2 years old. Children aged 2 years to 4 years without high risk conditions (see page 3) and with mild illness do not necessarily require antiviral treatment.
- Treatment, when indicated, should be initiated as early as possible because the benefits are greatest when started within the first 2 days of illness. However, some studies of hospitalized patients with seasonal and 2009 H1N1 influenza have suggested benefit of antiviral treatment even when treatment was started more than 48 hours after illness onset.
- To reduce delays in treatment initiation, consider:
 - 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.s
- 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 in detecting 2009 H1N1 has ranged 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.
- Consideration for antiviral chemoprophylaxis should generally be reserved for persons at higher risk for influenza-related complications who have had contact with someone likely to have been infected with influenza. However, early treatment is an emphasized alternative to chemoprophylaxis after a suspected exposure. Household or close contacts (with risk factors for influenza complications) of confirmed or suspected cases can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their healthcare provider for evaluation and possible early treatment if clinical signs or symptoms develop. Early recognition of illness and treatment when indicated is preferred to chemoprophylaxis for vaccinated persons after a suspected exposure.
- 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.
- 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/> (<http://www.cdc.gov/h1n1flu/eua/>)), subject to the terms and conditions of the EUA.

Objective

To provide updated recommendations 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 hospitalized patients and those at higher risk for influenza-related complications. The healthcare provider's assessment of a patient's clinical presentation as well as underlying risk factors is always an essential part of decisions about the need for further medical evaluation or treatment.

These recommendations can be adapted according to local epidemiologic data, antiviral susceptibility patterns, and antiviral supply considerations. These recommendations may be further revised if changes in the clinical presentation or antiviral susceptibility of 2009 H1N1 influenza are observed. Additional information about these recommendations can be found in [Questions and Answers: Revised Recommendations for the Use of Influenza Antiviral Drugs](http://www.cdc.gov/h1n1flu/antiviral.htm) (<http://www.cdc.gov/h1n1flu/antiviral.htm>).

Background

As of October 3, 2009, 99% 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. Based on currently available data, approximately 70% of persons hospitalized with 2009 H1N1 influenza have had a recognized high risk condition. These groups are similar to those who are at increased risk for seasonal influenza-related complications:

- Children younger than 2 years old;
- Adults 65 years of age or older
- Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss)
- Persons with the following conditions:
 - Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), or metabolic disorders (including diabetes mellitus);
 - Disorders that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders)
 - Immunosuppression, including that caused by medications or by HIV;

Rates of influenza-associated hospitalization from 2009 H1N1 have varied by age group. The risk of influenza-associated hospitalizations in children younger than 2 years old is equal to or greater than the risk of other high-risk groups. During April through September 2009 hospitalization rates for laboratory-confirmed 2009 H1N1 influenza based on the [Emerging Infections Program](http://www.cdc.gov/flu/weekly) (www.cdc.gov/flu/weekly) laboratory confirmed influenza hospitalizations surveillance system, among children younger than 2 years old were 2.3 times higher than rates for children 2 year to 4 years old. Children 2 years to 4 years old had slightly (20%) higher rates

of hospitalization compared with children 5 years to 17 years old. Hospitalization rates among children younger than 2 years of age were 4.5 times higher than that for adults and hospitalization rates of 2-4 year olds and 5-17 year olds were 2 times and 1.6 times higher, respectively, compared to adults. In pediatric studies of seasonal influenza, the risk for hospitalization is also highest for infants, with the risk decreasing as age increases. Given this increased risk for hospitalization, children younger than 2 years old are generally recommended for antiviral treatment. Children ages 2 and older and adults less than 65 years of age without high risk conditions (see above) and who are not severely ill do not necessarily require antiviral treatment. Healthcare providers should use clinical judgment to guide treatment decisions. Children and adults of any age presenting with suspected influenza and symptoms of lower respiratory tract illness or clinical deterioration should receive prompt empiric antiviral therapy in addition to other indicated treatment (e.g. antibiotics if bacterial co-infection is suspected). Updated information on hospitalization rates by age group can be found at www.cdc.gov/flu/weekly (<http://www.cdc.gov/flu/weekly>).

Persons 65 years and older are less likely to become ill with 2009 H1N1 influenza compared to younger persons. However, when persons aged 65 years or older acquire influenza, they are at higher risk for severe influenza-related complications.

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 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5601a1.htm>) 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 October 3, 2009, 99% 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 (#table1)).

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. Most healthy persons who develop suspected or confirmed 2009 H1N1 influenza or seasonal influenza who present with an uncomplicated febrile illness generally do not require antiviral treatment. In addition, persons who appear to be recovering from influenza generally do not require antiviral 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. Early empiric treatment should be considered for outpatients who are at higher risk for influenza-related complications (see above). Clinical judgment should be used in deciding whether outpatients with risk factors for influenza-related complications require treatment.
3. Treatment with oseltamivir or zanamivir is recommended for persons with suspected or confirmed influenza who have evidence of severe illness such as signs or symptoms of lower respiratory tract infection or clinical deterioration. Evidence of severe illness due to suspected influenza is an indication for immediate antiviral treatment, regardless of previous health or age. Clinicians are also reminded to consider the possibility of bacterial coinfections that can occur during or after an influenza illness.
4. 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-based testing could 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”](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5830a2.htm) (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5830a2.htm>) 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 developing severe disease is likely to be highest among infants and younger children. Once the decision to administer antiviral treatment is made by the healthcare 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 or 2009 H1N1 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 \(#table1\)](#)). 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. The U.S. Food and Drug Administration (FDA) has authorized oseltamivir use for children younger than 1 year old under an Emergency Use Authorization (EUA) in response to the current public health emergency involving 2009 H1N1 influenza virus. The use of oseltamivir is subject to the terms and conditions of the EUA. 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 \(#table2\)](#)) ([See Emergency Use Authorization of Tamiflu \(oseltamivir\) \(/h1n1flu/eua/tamiflu.htm\)](#)).

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, healthcare 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 who have illnesses compatible with influenza and are 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 and additional medical evaluation can be arranged if needed;
4. Request that patients at higher risk for influenza complications contact the provider if signs or symptoms of influenza develop, obtain medication as quickly as possible if prescribed by the provider, and initiate treatment. Providers should take into account

patient reliability, ability to understand the information about symptoms of influenza, and access to a pharmacy when considering ways to reduce treatment delays.

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 healthcare consultation if symptoms recur.

In October 2009, monovalent inactivated and live attenuated 2009 H1N1 influenza vaccines (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5839a3.htm>) became available in the United States. These vaccines are prepared using methods similar to those used for seasonal influenza vaccines. Although these vaccines are expected to be highly effective, no vaccine is 100% efficacious. Therefore, a history of receipt of 2009 H1N1 or seasonal influenza vaccine does not rule out influenza infection. Early empiric treatment should be initiated for vaccinated persons with suspected influenza infection when indicated (e.g. persons requiring hospitalization, with severe infection, or at higher risk for influenza-related complications). Vaccination with 2009 H1N1 influenza vaccine is not expected to provide protection against infection with seasonal influenza A or B viruses. Similarly, vaccination with seasonal influenza vaccine is not expected to prevent infection with 2009 H1N1 influenza virus.

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 Taking Care of a Sick Person in Your Home (http://www.cdc.gov/h1n1flu/guidance_homecare.htm) and Physician Directions to Patient/Parent (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 zanamivir, 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](#) (<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, and persons who are immune compromised can shed influenza virus for longer periods. However, the amount of virus shed generally correlates with magnitude of fever. For these recommendations, 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.
 - Healthcare 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](#) (http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm) 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 \(#table1\)](#)). 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 \(/h1n1flu/eua/\)](#) 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 recognition of illness and treatment as an alternative to chemoprophylaxis after a suspected exposure. Persons with risk factors for influenza complications who are household or close contacts of confirmed or suspected cases, and healthcare personnel who have occupational exposures, can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their healthcare provider for evaluation and early treatment when indicated if clinical signs or symptoms develop. Healthcare providers should use clinical judgment regarding situations where early recognition of illness and treatment might be an appropriate alternative to chemoprophylaxis. Early recognition of illness and treatment when indicated is preferred to chemoprophylaxis for healthy vaccinated persons, including healthcare workers, after a suspected exposure.

Persons at ongoing occupational risk for exposure (e.g., healthcare personnel, public health workers, or first responders who are working in communities with influenza outbreaks) should carefully follow guidelines for appropriate personal protective equipment. Efforts to reduce the risk of exposure or infection for healthcare personnel should include appropriate administrative controls (e.g. having healthcare personnel stay home from work when ill, and triaging for identification of potentially infectious patients), cough and hand hygiene, personal protective equipment, and vaccination when available.

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> (<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 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.htm>). 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 2009 H1N1 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 (<http://www.cdc.gov/flu/professionals/infectioncontrol/institutions.htm>).

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 large numbers of 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), 2008 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr57e717a1.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  (<http://www.journals.uchicago.edu/doi/pdf/10.1086/598513>)  (<http://www.journals.uchicago.edu/doi/pdf/10.1086/598513>)
3. Interim Guidance for Correctional and Detention Facilities on Novel Influenza A (H1N1) Virus (http://www.cdc.gov/h1n1flu/guidance/correctional_facilities.htm)
4. Interim Guidance for Homeless and Emergency Shelters on the Novel Influenza A (H1N1) Virus (<http://www.cdc.gov/h1n1flu/guidance/homeless.htm>)

(<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 healthcare 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 or are of an age 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 product information for Tamiflu® and Relenza®)

| Medication | | Treatment (5 days) | Chemoprophylaxis (10 days) |
|--|-------------------|--|---|
| Oseltamivir | | | |
| Adults | | | |
| | | 75-mg capsule twice per day | 75-mg capsule once per day |
| Children ≥ 12 months | | | |
| Body Weight (kg) | Body Weight (lbs) | | |
| ≤15 kg | ≤33lbs | 30 mg twice daily | 30 mg once per day |
| > 15 kg to 23 kg | >33 lbs to 51 lbs | 45 mg twice daily | 45 mg once per day |
| >23 kg to 40 kg | >51 lbs to 88 lbs | 60 mg twice daily | 60 mg once per day |
| >40 kg | >88 lbs | 75 mg twice daily | 75 mg once per day |
| Zanamivir | | | |
| Adults | | | |
| | | 10 mg (two 5-mg inhalations) twice daily | 10 mg (two 5-mg inhalations) once daily |
| Children (≥7 years or older for treatment, ≥5 years for chemoprophylaxis) | | | |
| | | 10 mg (two 5-mg inhalations) twice daily | 10 mg (two 5-mg inhalations) once daily |

Healthcare providers and pharmacists should be aware that an oral dosing dispenser with 30 mg, 45 mg, and 60 mg graduations is provided with TAMIFLU® for Oral Suspension, rather than graduations in milliliters (mL) or teaspoons (tsp). There have been cases where the units of measure on the prescription instructions (mL, tsp) do not match the units on the dosing device (mg), which has led to patient or caregiver confusion and dosing errors. When dispensing commercially manufactured TAMIFLU® for Oral Suspension, pharmacists should ensure the units of measure on the prescription instructions match the dosing device. If prescription instructions specify administration using milliliters (mL) or teaspoons (tsp), then

the device included in the Tamiflu® product package should be removed and replaced with an appropriate measuring device, such as an oral syringe if the prescribed dose is in milliliters (mL).

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 \(#table2\)](#) and [Emergency Use Authorization of Tamiflu \(oseltamivir\) \(<http://www.cdc.gov/h1n1flu/eua/tamiflu.htm>\)](#)).

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 |

Note to Prescribers: When commercially-manufactured Tamiflu® oral suspension is not available, oseltamivir 75 mg capsules can also be compounded at most retail pharmacies into a suspension. Health care providers can suggest this compounding alternative when writing prescriptions for Tamiflu® oral suspension. The Tamiflu® oral suspension concentration is 12 mg/mL; the compounded suspension concentration is 15 mg/mL. We advise prescribers to

specify the concentration (e.g. Tamiflu® oral suspension 12mg/mL) if prescribing in mL or teaspoons, or to prescribe the dose in milligrams (mg).

Note to Pharmacists: When dispensing Tamiflu® oral suspension for children younger than 1 year of age, the oral dosing dispenser that is included in the Tamiflu® package should always be removed as it only provides graduations in 30 mg, 45 mg, and 60 mg. An oral syringe that is capable of accurately measuring the prescribed dose in milliliters (mL) should be provided, and the caregiver counseled on how to administer the prescribed dose accurately with the oral syringe provided. For additional information refer to: http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm (http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm) and <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm183649.htm>  (<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm183649.htm>).

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). Healthcare 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>   (<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.

Anecdotal reports suggest that postpartum women, similar to pregnant women, might be at increased risk for severe complications and death from 2009 H1N1 influenza. These reports are consistent with the postpartum period being a time of transition to normal immune, cardiac, and respiratory function, a transition that is believed to occur quickly, but would be unlikely to occur immediately at delivery. Based on these reports, women should be considered to be at increased risk of influenza-related complications up to 2 weeks postpartum (including following pregnancy loss). Prompt empiric antiviral treatment is indicated for suspected or confirmed 2009 H1N1 influenza in women who are up to 2 weeks postpartum (including following pregnancy loss).

Adverse Events and Contraindications

Oseltamivir and zanamivir are generally well-tolerated. Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment (nausea without vomiting, approximately 10%; vomiting, approximately 9%) than among persons receiving placebo (nausea without vomiting, approximately 6%; vomiting, approximately 3%). Among children treated with oseltamivir, 14% had vomiting, compared with 8.5% of placebo recipients. Oseltamivir suspension is formulated with sorbitol, which may be associated with diarrhea and abdominal pain in patients who are fructose-intolerant.

Zanamivir, an inhaled medication, can induce bronchospasm and is not recommended for treatment for patients with underlying pulmonary disease. Zanamivir should only be used as directed in the prescribing information by using the Diskhaler device provided with the drug product. The commercial zanamivir formulation (Relenza® Inhalation Powder) is a mixture of zanamivir active drug substance and lactose drug carrier. This formulation is not designed or intended to be used in any nebulizer or mechanical ventilator as there is a risk that the lactose sugar can obstruct proper functioning of mechanical ventilator equipment. Although there are published and unpublished reports of zanamivir being used via nebulizer and mask in clinical trials, the currently available commercial formulation is not designed or intended to be administered by nebulization. Allergic reactions (rash, swelling of the face or tongue, anaphylaxis) have been reported in clinical practice with both oseltamivir and zanamivir. Rarely, transient neuropsychiatric events (self-injury or delirium) have been reported in postmarketing surveillance among persons taking oseltamivir and zanamivir. The majority of reports were among children and adolescents living in Japan. Because influenza infection itself can be associated with a variety of neurologic and behavioral symptoms, including seizures, delirium, and hallucinations, whether the neuraminidase inhibitors are directly responsible for these neuropsychiatric effects is unclear. To date, retrospective analyses conducted by Roche, the manufacturer of oseltamivir, have not found evidence for an increased risk of neuropsychiatric events after oseltamivir use. Until additional data are available, FDA advises

that persons receiving neuraminidase inhibitors be monitored for abnormal behavior. Health-care professionals should report all serious adverse events (SAE) after antiviral medication use promptly to MedWatch, the FDA's adverse event reporting program for medications (<http://www.fda.gov/medwatch/report/hcp.htm> [ⓧ](http://www.fda.gov/medwatch/report/hcp.htm) (<http://www.fda.gov/medwatch/report/hcp.htm>))

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) (<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) [ⓧ](http://www.idsociety.org/content.aspx?id=9202#flu) (<http://www.idsociety.org/content.aspx?id=9202#flu>)
- Jain, S et al. [Hospitalized Patients with 2009 H1N1 Influenza in the United States, April-June 2009.](http://h1n1.nejm.org/?p=979) [ⓧ](http://h1n1.nejm.org/?p=979) (<http://h1n1.nejm.org/?p=979>) *N Engl J Med* 2009;361. Available at: <http://content.nejm.org/cgi/reprint/NEJMoa0906695.pdf> [ⓧ](http://content.nejm.org/cgi/reprint/NEJMoa0906695.pdf) [ⓧ](http://content.nejm.org/cgi/reprint/NEJMoa0906695.pdf) (<http://content.nejm.org/cgi/reprint/NEJMoa0906695.pdf>)
- 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> (<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; 99 (S2): S248-S254.

Adverse events from influenza antiviral medications should be reported through the [U.S. FDA Medwatch website](http://www.fda.gov/medwatch/) [ⓧ](http://www.fda.gov/medwatch/) (<http://www.fda.gov/medwatch/>).

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Page last reviewed September 22, 2009 2:00 PM ET
Page last updated September 22, 2009 2:00 PM ET
Content source: [Centers for Disease Control and Prevention](http://www.cdc.gov)

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