



**Protocol for Outpatient Treatment and Prophylaxis
of H1N1 Influenza**

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A. Policy

It is the policy of Region 4 Public Health to assure access to public health and Strategic National Stockpile resources. Persons and populations at highest risk for morbidity and mortality have priority access to these resources.

B. Procedure

1. Health care provider determines need for antiviral treatment or prophylaxis based on criteria (See part C below).
2. Healthcare provider should report a suspected, probable or confirmed case at 360-397-8021 or toll free at 1-877-510-2772 to.
3. Healthcare provider requesting consultation should call 360-397-8021 or toll free at 1-877-510-2772 to speak with an epidemiologist or a public health nurse.
4. Healthcare provider fills out prescription indicating in writing:
 - a. Purpose of prescription (“for (treatment/prophylaxis) of (suspected/probable/confirmed)H1N1”)
 - b. The provider’s clinical documentation should include information demonstrating that the patient meets one or more of the criteria for prophylaxis or treatment. Clinical documentation does not need to be submitted.
5. Patient takes the prescription to a participating pharmacy, including provider office pharmacies when available. Participating pharmacies are pharmacies that have signed a memorandum (see Appendix A) stating that they have agreed to dispense Local Health Jurisdiction (LHJ)-supplied antiviral medication at no cost contingent on the provider following this protocol.
6. Pharmacy fills prescription.



7. Pharmacy keeps record (See Appendix B) of medications dispensed, reasons for dispensing (prophylaxis or treatment) and faxes record to LHJ weekly.

C. Criteria for Treatment

1. Suspect, Probable or Confirmed case (see case definitions below) AND is in high risk category (see number 2 below) AND is deemed clinically stable and therefore appropriate to treat as an outpatient.
 - a. Clinically unstable patients are defined as those with any of the following: increased respiratory rate, tachycardia, poor fluid intake, dehydration, or exacerbation of underlying chronic disease including but not limited to asthma, CHF, emphysema/COPD, asthma, HIV, or other immune disorder. Clinically unstable patients should be referred to the nearest emergency department.
 - b. Individuals who are stable, with mild disease, and NOT high risk do not require treatment.
2. Categories associated with a high risk for complications:
 - a. <5 years or > 65 years of age
 - b. Has asthma or other chronic pulmonary diseases, such as cystic fibrosis in children or chronic obstructive pulmonary disease in adults
 - c. Has hemodynamically significant cardiac disease
 - d. Has an immunosuppressive disorder or is receiving immunosuppressive therapy
 - e. Is infected with HIV
 - f. Pregnant women
 - g. Has sickle cell anemia or another hemoglobinopathy
 - h. Has an illness that requires long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
 - i. Has chronic renal dysfunction
 - j. Has cancer
 - k. Has a chronic metabolic disease, such as diabetes mellitus
 - l. Has a neuromuscular disorder, seizure disorder, or cognitive dysfunction that may compromise the handling of respiratory secretions
 - m. Is a resident of a nursing home or other long-term care facility

C. Criteria for Prophylaxis

1. Household or close contacts of a confirmed or probable case who are at high-risk for complications of influenza (see list above).
2. Health care workers or public health workers who were not using appropriate personal protective equipment during close contact with an ill confirmed, probable, or suspect case of swine-origin influenza A (H1N1) virus infection during the case's infectious period.

D. Case Definitions



1. A **confirmed case** of S-OIV infection is defined as a person with an acute febrile respiratory illness with laboratory confirmed S-OIV infection at CDC by one or more of the following tests:
 - a. real-time RT-PCR
 - b. viral culture
2. A **probable case** of S-OIV infection is defined as a person with an acute febrile respiratory illness who is positive for influenza A, but negative for H1 and H3 by influenza RT-PCR
3. A **suspect case** of S-OIV infection is defined as a person with acute febrile respiratory illness, defined as cough or sore throat or rhinorrhea or nasal congestion AND measured temp > 37.8C (>100 F).

E. Antiviral Treatment

The **swine** influenza A (H1N1) virus is sensitive (susceptible) to the neuraminidase inhibitor antiviral medications zanamivir and oseltamivir. It is resistant to the adamantane antiviral medications, amantadine and Rimantadine. Recommendations for use of antivirals may change as data on antiviral effectiveness, clinical spectrum of illness, adverse events from antiviral use, and antiviral susceptibility data become available.

Antiviral treatment with zanamivir or oseltamivir should be initiated as soon as possible after the onset of symptoms. Evidence for benefits from treatment in studies of seasonal influenza is strongest when treatment is started within 48 hours of illness onset. However, some studies of treatment of seasonal influenza have indicated benefit, including reductions in mortality or duration of hospitalization even for patients whose treatment was started more than 48 hours after illness onset. Recommended duration of treatment is five days.

Antiviral doses recommended for treatment of swine-origin influenza A (H1N1) virus infection in adults or children 1 year of age or older are the same as those recommended for seasonal influenza ([Table 1](#)). Oseltamivir use for children < 1 year old was recently approved by the U.S. Food and Drug Administration (FDA) under an Emergency Use Authorization (EUA), and dosing for these children is age-based ([Table 2](#)).

Note: Regional epidemiology demonstrates that circulating Seasonal Influenza H1N1 (as opposed to swine-origin H1N1) may be oseltamivir-resistant. Therefore, the treatment of choice for cases (as providers will generally not be able to distinguish seasonal Influenza A from swine-origin Influenza A when initiating treatment) will be either

- **Zanamivir (Relenza) alone OR**
- **Oseltamivir (Tamiflu) plus Rimantadine**
 - i. **Oseltamavir plus Rimantadine is the treatment of choice for patients with COPD and asthma**



The decision to treat is purely clinical. It is not necessary or desirable to wait for laboratory confirmation in an individual who requires hospitalization or is in a high risk category.

Important patient education should include the following information:

- Antiviral medications do not “cure” the flu. They will probably shorten the course of illness and decrease risk of serious complications. They do NOT reduce or prevent transmission.
- Side effects and drug interaction
 - Oseltamivir: 2-15% may experience GI side effects (nausea, vomiting, diarrhea); < 1% allergy, anaphylaxis.
 - Rimantadine: limited side effects noted.
 - Zanamavir: Caution in patients with respiratory conditions. Side effects include headache, cough, brochospasm, GI symptoms.
- Followup instructions
 - Return to clinic or ER for symptoms including but not limited to
 - Cough or fever not resolving, increased respiratory distress, decreased or inability to take fluids, vomiting.
- Review respiratory precautions at home, advise patients to stay home for at least 7 days after onset of symptoms or 24 hours after symptoms resolve to prevent transmission.

F. Antiviral Prophylaxis

For antiviral chemoprophylaxis of swine-origin influenza A (H1N1) virus infection, either oseltamivir or zanamivir are recommended (Table 1). Duration of antiviral chemoprophylaxis *post-exposure* is 10 days after the last known exposure to an ill confirmed case of swine-origin influenza A (H1N1) virus infection. Post exposure prophylaxis should be considered for contact during the *infectious period* (e.g., one day before until 7 days after the case’s onset of illness). If the contact occurred more than 7 days earlier, then prophylaxis is not necessary. Oseltamivir can also be used for chemoprophylaxis under the EUA (Table 3).

F. Special Considerations: Infants and Pregnant Women:

Infants:

Children under one year of age are at high risk for complications from seasonal human influenza virus infections. The characteristics of human infections with swine-origin H1N1 viruses are still being studied, and it is not known whether infants are at higher risk for complications associated with swine-origin H1N1 infection compared to older children and adults. Limited safety data on the use of oseltamivir (or zanamivir) are available from children less than one year of age, and oseltamivir is not licensed for use in children less than 1 year of age. Available data come from use of oseltamivir for treatment of seasonal influenza. These data suggest that severe adverse events are rare, and the Infectious Diseases Society of America recently noted, with regard to use of oseltamivir in children younger than 1 year old with seasonal influenza, that "...limited



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retrospective data on the safety and efficacy of oseltamivir in this young age group have not demonstrated age-specific drug-attributable toxicities to date."

Because infants typically have high rates of morbidity and mortality from influenza, infants with swine-origin influenza A (H1N1) infections may benefit from treatment using oseltamivir. 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 swine-origin H1N1 influenza or who has been exposed to a confirmed swine H1N1 case, and carefully monitor infants for adverse events when oseltamivir is used.

Pregnant Women

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. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, oseltamivir or zanamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus; the manufacturers' package inserts should be consulted. However, no adverse effects have been reported among women who received oseltamivir or zanamivir during pregnancy or among infants born to women who have received oseltamivir or zanamivir. 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 prophylaxis 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.



H. Tables

Table 1: Antiviral Dosing

Agent, group		Treatment (5 Days)	Chemoprophylaxis (10 days)
Oseltamivir			
Adults		75 - mg capsule twice per day	75 - mg capsule once per day
Children (age, 12 months or older), weight:	15 kg or less	60 mg per day divided into 2 doses	30 mg once per day
	15–23 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
	>40 kg	150 mg per day divided into 2 doses	75 mg once per day
Zanamivir			
Adults		Two 5 - mg inhalations (10 mg total) twice per day	Two 5 - mg inhalations (10 mg total) once per day
Children		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)

Pregnancy- 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. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, oseltamivir or zanamivir should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

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

Age	Recommended treatment dose for 5 days
<3 months	12 mg twice daily
3-5 months	20 mg twice daily
6-11 months	25 mg twice daily

Table 3: Dosing recommendations for antiviral chemoprophylaxis of children younger than 1 year using oseltamivir.



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

Table 3: Dosing recommendations for antiviral treatment of adults using Rimantadine.

Age group	Treatment (5 Days)
Adults	
<65 years	100 mg twice daily
>65 years	100 mg once daily

A reduction in dosage to 100 mg/day of Rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance less than 10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of Rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider Rimantadine appropriate for treatment among children. Studies evaluating the efficacy of Rimantadine in children are limited, but they indicate that treatment with either Rimantidine or oseltamavir diminishes the severity of influenza A infection when administered within 48 hours of illness onset.