# Influenza Management Guide 2009-2010 (UPDATED October 27, 2009)

**National HIV/AIDS Clinicians’ Consultation Center — Warmline 1-800-933-3413**

As a living document, this Table was last reviewed and updated November 2, 2009. Latest PDF available at www.nccc.ucsf.edu.

**Document authored by Mina Matin, MD and Ronald H. Goldschmidt, MD**

Note: Refer to the weekly influenza surveillance report provided by the CDC Influenza Division for the most up to date information: [http://www.cdc.gov/flu/weekly/](http://www.cdc.gov/flu/weekly/)

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<table>
<thead>
<tr>
<th>BACKGROUND</th>
<th>2009 H1N1 Flu (“Swine Flu”)</th>
<th>Seasonal Flu</th>
<th>Notes</th>
<th>Special considerations for HIV positive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Culprit viruses</strong></td>
<td>• 2009 H1N1 also known as: - 2009 pandemic Influenza A - H1N1 - Novel Influenza A</td>
<td>• Seasonal H1N1 and H3N2</td>
<td>• In previous years Seasonal Influenza circulation has dominated primarily in the winter months.</td>
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<tr>
<td><strong>Route of transmission</strong></td>
<td>Direct contact with secretions and airborne droplets</td>
<td>Direct contact with secretions and airborne droplets</td>
<td>Aerosol is a possible route of transmission, although limited to short distances of possibly a few feet.</td>
<td>• Wash hands often. Alcohol-based hand sanitizer when soap and water not available.</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Abrupt onset of influenza-like illness: e.g., fever, cough, sore throat, rhinorrhea, congestion, headaches, myalgia, nausea, vomiting, diarrhea.</td>
<td>Abrupt onset of influenza-like illness: e.g., fever, cough, sore throat, rhinorrhea, congestion, headache, myalgia.</td>
<td>Nausea, vomiting and diarrhea reported more frequently with 2009 H1N1 Flu than Seasonal Flu.</td>
<td>• Avoid touching face, especially eyes, nose or mouth.</td>
</tr>
<tr>
<td><strong>Persons most susceptible to infection</strong></td>
<td>Babies, children, teens, and young adults</td>
<td>Babies, children, elderly</td>
<td>Infants and young children at highest risk of severe disease with 2009 H1N1.</td>
<td>• Maintain healthy lifestyle: e.g., balanced diet, sleep hygiene, reduce stress.</td>
</tr>
</tbody>
</table>

Influenza-like illness in-season: ~ 80% influenza etiology. Influenza-like illness out-of-season: < 40% influenza etiology.

Infants < 6 mo not candidates for vaccination. If possible, adults who are not sick should care for infants, including feedings—pumped milk. Note: risk of influenza transmission through breast milk is unlikely; reports of viremia with Seasonal Flu are rare, suggesting that risk of virus crossing into breast milk probably is rare.

HIV positive patients at higher risk of influenza-related complications; course of illness might be prolonged. Those with low CD4 counts are at higher risk for lower respiratory tract infections and recurrent pneumonias.

HIV positive patients are **NOT** at increased risk of acquiring influenza compared with their uninfected peers, although they are at higher risk of influenza-related complications.

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The National HIV/AIDS Clinicians’ Consultation Center (NCCC) in the University of California, San Francisco (UCSF) Department of Family & Community Medicine at San Francisco General Hospital, is funded by the Health Resources and Services Administration (HRSA) AIDS Education and Training Centers (AETCs) Grant No. H4AHA01082 and receives additional funding from the Centers for Disease Control and Prevention (CDC).
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</thead>
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<tr>
<td>Highest rates of hospitalization and deaths</td>
<td>• Pregnant women&lt;br&gt;• Young children &lt; 4 yo, especially those &lt; 2 yo&lt;br&gt;• Obese patients (BMI &gt; 35)&lt;br&gt;• Adults &gt; 50 yo</td>
<td>Adults &gt; 65 yo</td>
<td>• Seasonal Flu: in past years the etiology of deaths has usually been bacterial superinfections, most commonly staphylococcal pneumonia. &lt;br&gt;• 2009 H1N1 Flu: etiology of deaths this year has in many cases been bacterial superinfections, most commonly pneumococcal pneumonia. A minority of patients with indications for pneumococcal vaccination have actually been vaccinated. Ensure all patients with indications are vaccinated.</td>
<td>• Historically HIV positive patients have had higher hospitalization rates, prolonged illness, and increased mortality from Seasonal Flu, especially among the more immunosuppressed. Assumed to be at higher risk for complications of 2009 H1N1 Flu. &lt;br&gt;Ensure that HIV positive patients are up to date on pneumococcal vaccinations.</td>
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<tr>
<th>DIAGNOSIS</th>
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<tr>
<td>Testing</td>
<td>• Screening test: RIDT (rapid influenza diagnostic test)—enzyme assay; sensitivity 10% to 70%&lt;br&gt;• Diagnostic tests:&lt;br&gt;  (a) real-time Reverse Transcriptase PCR (rRT-PCR)&lt;br&gt;  (b) culture (expensive)</td>
<td>• Screening test: RIDT (rapid influenza diagnostic test)—enzyme assay; sensitivity 20% to 70%&lt;br&gt;• Diagnostic tests:&lt;br&gt;  (a) real-time Reverse Transcriptase PCR (rRT-PCR)&lt;br&gt;  (b) culture (expensive)</td>
<td>• Testing usually not warranted; management is by clinical presentation. Testing generally restricted to settings where management is impacted: e.g., in hospitalizations where isolation of patient with influenza would be required. &lt;br&gt;• Utility of RIDT is limited: low sensitivity, low specificity. False negative results are common. &lt;br&gt;• RIDT can distinguish between Influenza A and B. Cannot distinguish between subtypes of Influenza A (i.e., 2009 H1N1 versus Seasonal H1N1). &lt;br&gt;• rRT-PCR is 98% sensitive and specific for Influenza A; if result is positive for Influenza A and negative for Seasonal H1 and H3, sample should be sent to qualified laboratory for confirmatory testing for 2009 H1N1 virus.</td>
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<th>TREATMENT</th>
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<tr>
<td>Chemoprophylaxis</td>
<td>Neuraminidase Inhibitor x 10 days after last known exposure.  Dosing information below</td>
<td>Combination of Neuraminidase Inhibitor and Adamantane x 10 days after last known exposure.  Dosing information below</td>
<td>• Note: Early Empiric Treatment is favored over chemoprophylaxis to avoid resistance. Early empiric treatment focuses on ensuring that patients at high risk of complications from influenza have access to antiviral medications without delay. &lt;br&gt;• Chemoprophylaxis generally is not recommended if &gt; 48 hours past last contact with an infectious person. &lt;br&gt;• In past years, due to high incidence of oseltamivir resistance, a combination regimen of oseltamivir and adamantane has been preferred for treatment of Seasonal Flu. As of October 2009 the vast majority of circulating virus was 2009 H1N1 with rare resistance to oseltamivir. At this time, chemoprophylaxis, if indicated, should empirically be choice of neuraminidase inhibitor WITHOUT adamantane. Combination of neuraminidase with adamantane is not indicated.</td>
<td></td>
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<tr>
<td>Early Empiric Treatment recommended</td>
<td>2009 H1N1 Flu (“Swine Flu”)</td>
<td>Seasonal Flu</td>
<td>Notes</td>
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<tr>
<td>Treat with neuraminidase inhibitor</td>
<td>Neuraminidase Inhibitor options:</td>
<td>Neuraminidase Inhibitor options:</td>
<td>Most healthy patients with no risk factors for complications recover without antiviral medications.</td>
<td>• HIV positive patients with influenza-like illness, or who are close contacts of persons with probable or confirmed influenza, can be considered for early empiric treatment versus chemoprophylaxis, particularly if they are at later stages of HIV disease or with advancing immunosuppression.</td>
</tr>
</tbody>
</table>
| a 5 days | → Oseltamivir = Tamiflu®  
• Dosing information below (oral pill, and liquid)  
• approved for patients > 1 yo  
• (FDA issued Emergency Use Authorization for patients < 1 yo) | → Oseltamivir = Tamiflu®  
• Dosing information below (oral pill, and liquid)  
• approved for patients > 1 yo  
• (FDA issued Emergency Use Authorization for patient < 1 yo) | Patients at high risk of influenza-related complications: | • Drug-drug interactions: Limited information on interactions between influenza antiviral and HIV antiretroviral drugs. No known absolute contraindications for co-administration of oseltamivir or zanamivir with currently available HIV antiretroviral medications. No adverse effects have been reported among HIV-infected adults and adolescents who have received oseltamivir or zanamivir. |
| Early empiric treatment of influenza-like-illness recommended for patients at high risk of influenza-related complications. | → Zanamivir = Relenza®  
• Dosing information below (inhaled powder)  
• approved for patients > 7 yo | → Zanamivir = Relenza®  
• Dosing information below (inhaled powder)  
• approved for patients > 7 yo | • Age < 2 yo  
• Pregnancy (up to 2 weeks postpartum, including pregnancy loss)  
• Age > 65 yo  
• Certain chronic medical conditions: e.g., lung disease (including asthma, COPD), cardiovascular (excluding hypertension), renal, hepatic, conditions with increased risk of aspiration, hematologic, or metabolic (e.g., diabetes)  
• Immunosuppression, including HIV  
• People younger than 19 years of age who are receiving long-term aspirin therapy (risk of Reye Syndrome)  
• Obesity (BMI > 35) | |
| Note: Goal of treatment is not to cure, but rather to reduce severity of illness and risk of influenza-related complications for patients at high risk. | → Peramivir (investigational)  
• Dosing information below (Intravenous formulation)  
• FDA issued Emergency Use Authorization October 2009 for patients who have failed or cannot tolerate the above oral or inhaled options.  
• Not an option if known oseltamivir resistance; caution if zanamivir resistance. | → SPECIAL CONSIDERATIONS:  
• Risk decreases if treated with antiviral drugs within 48 hours of symptom onset; may offer benefit after 48 hours.  
• Zanamivir can cause bronchial spasm; caution advised in patients with asthma or chronic lung disease. | • Hospitalized patients: treatment may be extended beyond 5 days for complicated illness. Some experts favor double dosing antivirals; risks and benefits not established.  
• Peramivir: option for severely-ill hospitalized patients with 2009 H1N1 (e.g. ICU); one-time IV treatment has also shown favorable results in clinical trials—currently Phase 3 trials underway; caution with renal insufficiency.  
• Pregnancies: Oseltamivir and zanamivir are “Pregnancy Category C” drugs. Pregnant women at high risk for complications—should receive prompt antiviral therapy. Pregnacy NOT a contraindication to antiviral treatment.  
• Breastfeeding: Treatment not contraindication to breastfeeding; pumped milk fed to infant by non-ill person.  
• HEALTH CARE PERSONNEL: consider chemoprophylaxis if unvaccinated and within 48 hours of unprotected close contact exposure to confirmed or suspected influenza.  
• Closed or semi-closed settings (e.g. nursing homes and some correctional facilities): implement chemoprophylaxis if exposure to known influenza where large numbers of persons at higher risk for influenza complications are housed. Generally does NOT include schools, camps or workplaces where outbreaks might occur.  
• Potential adverse effects of oseltamivir in children: nausea and vomiting. (Rare reports: delirium, self-injury among children in Japan after taking oseltamivir—unclear etiology.) | |
| See dosing information below. | → Adamantane  
• Amantadine | → Amantadine  
→ Rimantidine | • Note: As both 2009 H1N1 and Influenza B are resistant to adamantanes, and symptoms of both Seasonal and 2009 H1N1 Flu are similar, do not use adamantanes as a sole agent for chemoprophylaxis or treatment. | |
| | • As of October 2009, 99% of circulating H1N1 viruses were susceptible to oseltamivir and zanamivir. | | • Note: As both 2009 H1N1 and Influenza B are resistant to adamantanes, and symptoms of both Seasonal and 2009 H1N1 Flu are similar, do not use adamantanes as a sole agent for chemoprophylaxis or treatment. | |
| | • Resistance to oseltamivir (14 cases in US) usually occurred in patients previously exposed to oseltamivir. All were sensitive to zanamivir. | | • Seasonal H1N1 in previous years has shown significant resistance to oseltamivir. During winter months, when Seasonal Flu viruses are expected to increase, combined use of (oseltamivir and amantadine) OR (zanamivir) might be indicated. | |

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(Page 3 of 6)
## PREVENTION

### Vaccines:

Both 2009 H1N1 vaccines and Seasonal Flu vaccines come in a live attenuated intranasal form and an inactivated injectable form.

**Influenza antiviral drugs** taken from 48 hours before through 2 weeks after administration of the live attenuated inhaled formulation (but not the injectable inactivated formulation) can interfere with immune protection from the vaccine.

**Contraindications to both intranasal and injectable formulations** include severe or life-threatening allergies to hen eggs and a history of onset of Guillain-Barre syndrome during the 6 weeks after previous vaccination.

**Contraindications to intranasal vaccine** include age < 2 yo or > 50 yo, pregnancy, age < 19 yo on aspirin therapy (risk of Reye Syndrome), chronic illness including asthma/reactive airway disease, chronic lung disease, heart disease, diabetes, kidney failure, weakened immune system or taking immunosuppressive medications.

**Notes**

A single 15 microgram dose of 2009 H1N1 monovalent vaccine (the same dose that is used in the Seasonal Flu vaccine) induces a robust immune response in most healthy adults in 8 to 10 days.

Younger children age < 9 yo should receive a series of 2 doses of 2009 H1N1 monovalent vaccine, as has been the recommendation for first-time administration of trivalent Seasonal Flu vaccine for this age group.

Both 2009 H1N1 vaccine and Seasonal Flu vaccine can be administered on the same day but at different sites. Options are: 2 IM injections at different sites; or one intranasal vaccine and the other IM injection.

Do not administer both intranasal vaccines together, this can interfere with immune protection optimally provided by separating these vaccines.

Most common side effect of injected vaccine is soreness at the injection site. Other side effects include fever, body aches and fatigue after inoculation. Most common side effects of nasal vaccine include runny nose or nasal congestion, sore throats in adults and low grade fever in children 2 to 6 years old.

### 2009 H1N1 Flu (“Swine Flu”)

- One dose if ≥ 10 yo
- Two doses 3-4 weeks apart if 6 mo to 9 yo
- Do not vaccinate < 6 mo

ACIP (Advisory Committee on Immunization Practices) tiered plan prioritizes 5 target groups:

- Pregnancy
- Caretakers of infants < 6 mo
- Health-care personnel
- Age 25 yo to 64 yo with higher risk of influenza-related complications.

In case of vaccine shortage, ACIP prioritizes a subset of these five initial target groups for vaccination:

- Pregnant women,
- Caretakers of infants < 6 mo
- Health-care personnel who have direct contact with patients or infectious material,
- Age 6 mo to 4 yo, and
- Age 5 yo to 18 yo at higher risk of influenza-related complications.

Once vaccination demand for the five initial target groups has been met, expand vaccination efforts to all persons aged 25 yo to 64 yo.

Risk of influenza for age ≥ 65 yo is lower than in younger age groups. Expand vaccinations to ≥ 65 yo once demand for vaccine among younger persons is met.

### Seasonal Flu

- One dose if ≥ 9 yo
- Two doses 3-4 weeks apart if 6 mo to 8 yo (first-time administration, otherwise single dose sufficient)
- Do not vaccinate < 6 mo

ACIP (Advisory Committee on Immunization Practices) tiered plan prioritizes target groups in case of shortage:

- Pregnancy
- Caretakers of infants < 6 mo
- Age 6 mo to 18 yo
- Age > 50 yo
- Health-care personnel
- Adults at higher risk of influenza-related complications.

### Special Considerations for HIV positive patients

- The intranasal live attenuated influenza vaccines are contraindicated for HIV positive patients.
- Inactivated formulation (injectable vaccine) is preferred over live attenuated intranasal vaccine for close contacts (e.g., household members, healthcare workers) of patients with severe immunocompromise.
- Rates of transmission of vaccine virus have been found to range 0.6% - 2.4%, but are unlikely to result in symptomatic illness.
- HIV positive patients > 10 yo should be dosed once with the Seasonal Flu vaccine, and once with the 2009 H1N1 vaccine. Can be administered on the same day at different sites.
- HIV positive patients are among the priority groups to be vaccinated, regardless of CD4 count.

### Notes

- Persons with moderate to severe febrile illness should not be vaccinated until symptoms abate per CDC guidance.
- Most common side effect of injected vaccine is soreness at the injection site. Other side effects include fever, body aches and fatigue after inoculation. Most common side effects of nasal vaccine include runny nose or nasal congestion, sore throats in adults and low grade fever in children 2 to 6 years old.

### References

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The table below is from the following website:
http://www.cdc.gov/h1n1flu/recommendations.htm

<table>
<thead>
<tr>
<th>Medication</th>
<th>Treatment (5 days)</th>
<th>Chemoprophylaxis (10 days)</th>
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<tbody>
<tr>
<td><strong>Oseltamivir</strong> (oral)</td>
<td></td>
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<tr>
<td>Adults</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-mg capsule twice per day</td>
<td>75-mg capsule once per day</td>
<td></td>
</tr>
<tr>
<td><strong>Children ≥ 12 months</strong></td>
<td></td>
<td></td>
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<tr>
<td>Body Weight (kg)</td>
<td>Body Weight (lbs)</td>
<td></td>
</tr>
<tr>
<td>≤15 kg</td>
<td>≤33 lbs</td>
<td>30 mg twice daily</td>
</tr>
<tr>
<td>&gt;15 kg to 23 kg</td>
<td>&gt;33 lbs to 51 lbs</td>
<td>45 mg twice daily</td>
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<tr>
<td>&gt;23 kg to 40 kg</td>
<td>&gt;51 lbs to 88 lbs</td>
<td>60 mg twice daily</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>&gt;88 lbs</td>
<td>75 mg twice daily</td>
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<tr>
<td><strong>Zanamivir</strong> (inhaled)</td>
<td></td>
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<tr>
<td>Adults</td>
<td></td>
<td></td>
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<tr>
<td>10 mg (two 5-mg inhalations) twice daily</td>
<td>10 mg (two 5-mg inhalations) once daily</td>
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<tr>
<td><strong>Children (≥7 years or older for treatment, ≥5 years for chemoprophylaxis)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg (two 5-mg inhalations) twice daily</td>
<td>10 mg (two 5-mg inhalations) once daily</td>
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</table>

Health care 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 lead 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).

Adults: 600mg intravenously once daily for 5-10 days. Note: one-time IV treatment has also shown favorable results in clinical trials. Currently Phase 3 trials underway
Children < 18 yo have not been studied in clinical trials. Limited use under Emergency Use Authorization.
The table below is from the following website:
http://www.cdc.gov/h1n1flu/recommendations.htm

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

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

When dispensing TAMIFLU® for 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. Pharmacists and health care providers should provide an oral syringe that is capable of accurately measuring the prescribed milliliter (mL) dose, and counsel the caregiver how to administer the prescribed dose.

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 (CASY). 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.

Acknowledgements:
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The NCCC’s National HIV Telephone Consultation Service (Warmline), in response to the 2009 pandemic Influenza A (H1N1), offers healthcare providers expert clinical consultation on influenza management in patients affected by HIV. The Warmline is available at 800-933-3413 Monday through Friday, 9 a.m. - 8 p.m. Eastern Standard Time.

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