

Online Table A. Influenza Management Guide 2009-2010				
BACKGROUND	2009 H1N1 (Swine Flu)	Seasonal Influenza	Notes	Special Considerations for HIV-Positive Patients
Culprit viruses	Influenza A , specifically 2009 H1N1 , also known as 2009 pandemic influenza A, novel H1N1, novel influenza A, and swine flu	Influenza A , usually seasonal H1N1 (not 2009 H1N1) and H3N2 Influenza B As of October 2009, seasonal influenza viruses co-circulated at low levels with 2009 H1N1	In previous years, seasonal influenza circulation has dominated primarily in the winter months. In October 2009, 99% of subtyped influenza A was 2009 H1N1 . 2009 H1N1 seasonal circulation pattern is as of yet unclear.	
Route of transmission	Direct contact with secretions and airborne droplets	Direct contact with secretions and airborne droplets	Aerosol is a possible route of transmission, although limited to short distances of possibly a few feet. The infectious period begins 24 hours before symptom onset and extends to 24 hours after fever ends. Amount of viral shedding correlates with the magnitude of fever. Health care personnel precautions are extended: do not return to work until 24 hours after fever ends or seven days post onset of symptoms, whichever is later. Patients on antiviral treatment continue to be potentially infectious for up to four or more days after treatment initiation. N95 respirator recommended for health care personnel caring for known, probable, or suspected infected patients.	General instructions: Wash hands often. Use alcohol-based hand sanitizer when soap and water are not available. Avoid touching face, especially eyes, nose, or mouth. Avoid close contact with sick people. Maintain healthy lifestyle (e.g., balanced diet, sleep hygiene, reduced stress). Specific instructions for HIV-positive patients: Maintain adherence to HIV medications and antimicrobial prophylaxis against opportunistic infections.
Symptoms	Abrupt onset of influenza-like illness (e.g., fever, cough, sore throat, rhinorrhea, congestion, headaches, myalgias, nausea, vomiting, diarrhea)	Abrupt onset of influenza-like illness (e.g., fever, cough, sore throat, rhinorrhea, congestion, headaches, myalgias)	Nausea, vomiting, and diarrhea reported more frequently with 2009 H1N1 than seasonal influenza. Influenza-like illness in-season: approximately 80% influenza etiology. Influenza-like illness out-of-season: less than 40% influenza etiology.	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 of lower respiratory tract infections and recurrent pneumonias.
Persons most susceptible to infection	Infants, children, teenagers, and young adults	Infants, children, and older adults	Infants and young children at highest risk of severe disease with 2009 H1N1. Little is known about prevention of influenza in infants. Infants younger than 6 months are 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 influenza are rare, suggesting that risk of virus crossing into breast milk probably is rare.	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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Highest rates of hospitalization and deaths	Pregnant women Children younger than 4 years, especially those younger than 2 years Obese patients (BMI > 35 kg per m ²) Adults older than 50 years	Adults older than 65 years	Seasonal influenza: in past years, the etiology of deaths has usually been bacterial superinfections, most commonly staphylococcal pneumonia. 2009 H1N1: 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.	Historically, HIV-positive patients have had higher hospitalization rates, prolonged illness, and increased mortality from seasonal influenza, especially among the more immunosuppressed. These patients are assumed to be at higher risk of complications from 2009 H1N1. Ensure that HIV-positive patients are up-to-date on pneumococcal vaccinations.
DIAGNOSIS	2009 H1N1 (Swine Flu)	Seasonal Influenza	Notes	Special Considerations for HIV-Positive Patients
Testing	Screening test: rapid influenza diagnostic test (RIDT)—enzyme assay; sensitivity 10% to 70% Diagnostic tests: (a) real-time reverse transcriptase PCR (rRT-PCR) (b) culture (expensive)	Screening test: RIDT—enzyme assay; sensitivity 20% to 70% Diagnostic tests: (a) rRT-PCR (b) culture (expensive)	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). Utility of RIDT is limited: low sensitivity, low specificity. False-negative results are common. RIDT can distinguish between influenzas A and B. Cannot distinguish between subtypes of influenza A (i.e., 2009 H1N1 versus seasonal H1N1). 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.	
TREATMENT	2009 H1N1 (Swine Flu)	Seasonal Influenza	Notes	Special Considerations for HIV-Positive Patients
Chemoprophylaxis NOTE: Chemoprophylaxis is generally not recommended. See Early Empiric Treatment section below.	Neuraminidase inhibitor for 10 days after last known exposure (dosing information listed below)	Combination of neuraminidase inhibitor and an adamantane for 10 days after last known exposure (dosing information listed below)	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. Chemoprophylaxis generally is not recommended if more than 48 hours have passed since last contact with an infectious person. In past years, due to high incidence of oseltamivir (Tamiflu) resistance, a combination regimen of oseltamivir and an adamantane has been preferred for treatment of seasonal influenza. As of October 2009, the majority of circulating viruses were 2009 H1N1 with rare resistance to oseltamivir. At this time, chemoprophylaxis, if indicated, should empirically be choice of neuraminidase inhibitor WITHOUT an adamantane. Combination of neuraminidase and an adamantane is not indicated.	

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<p>Early Empiric Treatment</p> <p>Treat with neuraminidase inhibitor for five days</p> <p>Early empiric treatment of influenza-like illness recommended for patients at high risk of influenza-related complications.</p> <p>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.</p> <p>See dosing information below.</p>	<p>Neuraminidase Inhibitor options:</p> <p>Oseltamivir (Tamiflu) Dosing information below (oral pill, and liquid) Approved for patients older than 1 year FDA issued Emergency Use Authorization for patients younger than 1 year</p> <p>Zanamivir (Relenza) Dosing information below (inhaled powder) Approved for patients older than 7 years</p> <p>Peramivir (investigational) Dosing information below (IV formulation) FDA issued Emergency Use Authorization in October 2009 if treatment has been ineffective or patients cannot tolerate the above oral or inhaled options. Not an option if known oseltamivir resistance; caution if zanamivir resistance.</p> <p>NOTE: Because 2009 H1N1 and influenza B are resistant to adamantanes, and symptoms of seasonal influenza and 2009 H1N1 are similar, do not use adamantanes as a sole agent for chemoprophylaxis or treatment.</p> <p>As of October 2009, 99% of circulating H1N1 viruses were susceptible to oseltamivir and zanamivir.</p> <p>Resistance to oseltamivir (14 cases in U.S.) usually occurred in patients previously exposed to oseltamivir. All patients were sensitive to zanamivir.</p>	<p>Neuraminidase Inhibitor options:</p> <p>Oseltamivir Dosing information below (oral pill, and liquid) Approved for patients older than 1 year FDA issued Emergency Use Authorization for patients younger than 1 year</p> <p>Zanamivir Dosing information below (inhaled powder) Approved for patients older than 7 years</p> <p>Adamantane options: Amantadine (Symmetrel) Rimantadine (Flumadine)</p> <p>NOTE: Because 2009 H1N1 and influenza B are resistant to adamantanes, and symptoms of seasonal influenza and 2009 H1N1 are similar, do not use adamantanes as a sole agent for chemoprophylaxis or treatment.</p> <p>Seasonal influenza in previous years has shown significant resistance to oseltamivir. During winter months, when seasonal influenza viruses are expected to increase, combined use of oseltamivir and an amantadine OR zanamivir might be indicated.</p>	<p>Most healthy patients with no risk factors for complications recover without antiviral medications.</p> <p>Patients at high risk of influenza-related complications: Age younger than 2 years Pregnancy (up to two weeks postpartum, including pregnancy loss) Age older than 65 years 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 who are receiving long-term aspirin therapy (risk of Reye syndrome) Obesity (BMI > 35 kg per m²)</p> <p>SPECIAL CONSIDERATIONS: Risk decreases if treated with antiviral drugs within <u>48 hours</u> 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 five 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., patients in ICU); one-time IV treatment has also shown favorable results in clinical trials (currently, Phase 3 trials are underway); caution with renal insufficiency. Pregnancy: oseltamivir and zanamivir are labeled by the FDA as “Pregnancy Category C” drugs. Pregnant women at high risk of complications should receive prompt antiviral therapy. Pregnancy is NOT a contraindication to antiviral treatment. Breastfeeding: treatment is not a contraindication to breastfeeding; ideally, breast milk pumped and 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 of 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 of delirium, self-injury among children in Japan after taking oseltamivir—unclear etiology.</p>	<p>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.</p> <p>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.</p>

PREVENTION	2009 H1N1 (Swine Flu)	Seasonal Influenza	Notes	Special Considerations for HIV-Positive Patients
<p>Vaccines</p> <p>2009 H1N1 and seasonal influenza vaccines come in a live attenuated intranasal form and an inactivated injectable form.</p> <p>Influenza antiviral drugs taken from 48 hours before through two weeks after administration of the live attenuated inhaled formulation (but not the injectable formulation) can interfere with immune protection from the vaccine.</p>	<p>2009 H1N1 monovalent vaccine</p> <p>One dose if 10 years or older</p> <p>Two doses, three to four weeks apart if 6 months to 9 years of age</p> <p>Do not vaccinate patients younger than 6 months</p> <p>ACIP's tiered plan prioritizes five target groups: Pregnant women Caretakers of infants younger than 6 months Patients 6 months to 24 years of age Health care personnel Patients 25 to 64 years of age with higher risk of influenza-related complications</p> <p>In case of vaccine shortage, ACIP prioritizes a subset of these five initial target groups for vaccination: Pregnant women Caretakers of infants younger than 6 months Health care personnel who have direct contact with patients or infectious material Patients 6 months to 4 years of age Patients 5 to 18 years of age who are at higher risk of influenza-related complications</p> <p>Once vaccination demand for the five initial target groups has been met, expand vaccination efforts to all persons 25 to 64 years of age.</p> <p>Risk of influenza for persons older than 65 years is lower than in younger age groups. Expand vaccinations to those 65 years or older once demand for vaccine among younger persons is met.</p>	<p>Seasonal influenza trivalent vaccine inclusive of seasonal H1N1 (not 2009 H1N1), H3N2, and influenza B</p> <p>One dose if 9 years or older</p> <p>Two doses, three to four weeks apart if 6 months to 8 years of age (first-time administration, otherwise single dose sufficient)</p> <p>Do not vaccinate patients younger than 6 months</p> <p>ACIP's tiered plan prioritizes target groups in case of shortage: Pregnant women Caretakers of infants younger than 6 months Patients 6 months to 18 years of age Patients older than 50 years Health care personnel Adults at higher risk of influenza-related complications</p>	<p>A single 15-mcg dose of 2009 H1N1 monovalent vaccine (the same dose that is used in the seasonal influenza vaccine) induces a robust immune response in most healthy adults in 8 to 10 days.</p> <p>Children younger than 9 years should receive a series of two doses of H1N1 2009 monovalent vaccine, as has been the recommendation for first-time administration of trivalent seasonal influenza vaccine for this age group.</p> <p>2009 H1N1 and seasonal influenza vaccines can be administered on the same day but at different sites. Options are: two IM injections at different sites; or one intranasal vaccine and the other an IM injection.</p> <p>Do not administer both intranasal vaccines together; this can interfere with immune protection optimally provided by separating these vaccines.</p> <p>Most common adverse effect of injected vaccine is soreness at the injection site. Other adverse effects include fever, body aches, and fatigue after inoculation. Most common adverse effects of nasal vaccine include runny nose or nasal congestion, sore throats in adults and low-grade fever in children 2 to 6 years of age.</p> <p>Contraindications to intranasal vaccine include age younger than 2 years or older than 50 years, pregnancy, age younger than 19 years 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.</p> <p>Contraindications to intranasal and injectable formulations include severe or life-threatening allergies to hen eggs and a history of onset of Guillain-Barré syndrome during the six weeks after previous vaccination.</p> <p>Persons with moderate to severe febrile illness should not be vaccinated until symptoms abate per CDC guidance.</p>	<p>The intranasal live attenuated influenza vaccines are contraindicated for HIV-positive patients.</p> <p>Inactivated formulation (injectable vaccine) is preferred over live attenuated intranasal vaccine for close contacts (e.g., household members, health care personnel) of patients with severe immunocompromise. Rates of transmission of vaccine virus have been found to range from 0.6% to 2.4%, but are unlikely to result in symptomatic illness.</p> <p>HIV-positive patients older than 10 years should receive one seasonal and one 2009 H1N1 vaccine. Can be administered on the same day at different sites.</p> <p>HIV-positive patients are among the priority groups to be vaccinated, regardless of CD4 count, in the setting of vaccine shortage.</p>

NOTE: As a living document, this table was last reviewed and updated October 27, 2009. This guide will continue to be updated throughout the 2009-2010 influenza season. The latest PDF version of this table is available at <http://www.nccc.ucsf.edu>. Also, please refer to the weekly influenza surveillance report provided by the CDC's Influenza Division for the most up-to-date information at <http://www.cdc.gov/flu/weekly>.

ACIP = Advisory Committee on Immunization Practices; BMI = body mass index; CDC = Centers for Disease Control and Prevention; COPD = chronic obstructive pulmonary disease; FDA = U.S. Food and Drug Administration; HIV = human immunodeficiency virus; ICU = intensive care unit; IM = intramuscular; IV = intravenous; PCR = polymerase chain reaction; RIDT = rapid influenza diagnostic test; rRT = real-time reverse transcriptase.

Adapted with permission from Matin M, Goldschmidt RH. Influenza Management Guide 2009-2010. 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. 2009.

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The NCCC's National HIV Telephone Consultation Service (Warmline), in response to the influenza pandemic, offers health care professionals expert clinical consultation on influenza management in patients affected by HIV. The Warmline is available at 1-800-933-3413, Monday through Friday, 9 a.m. to 8 p.m. Eastern Standard Time.

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Online Table B. Dosing Recommendations for Antiviral Treatment or Chemoprophylaxis of 2009 H1N1 Infection		
Medication	Treatment (5 days)	Chemoprophylaxis (10 days)
Oseltamivir (Tamiflu), oral		
Adults		
	75-mg capsule twice daily	75-mg capsule once daily
Children ≥ 12 months		
Body weight		
≤ 15 kg (33 lb)	30 mg twice daily	30 mg once daily
> 15 to 23 kg (33 to 51 lb)	45 mg twice daily	45 mg once daily
> 23 to 40 kg (51 to 88 lb)	60 mg twice daily	60 mg once daily
> 40 kg (88 lb)	75 mg twice daily	75 mg once daily
Zanamivir (Relenza), inhaled		
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 or older for chemoprophylaxis)		
	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily
Peramivir, intravenous		
Adults*		
	600 mg IV once daily for five to 10 days†	

NOTE: Health care professionals 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).

FDA = U.S. Food and Drug Administration; IV = intravenous.

*—Children younger than 18 years have not been studied in clinical trials. Limited use under FDA Emergency Use Authorization (<http://www.cdc.gov/h1n1flu/eua/peramivir.htm>).

†—One-time IV treatment has also shown favorable results in clinical trials. Phase 3 trials are underway.

Adapted from Centers for Disease Control and Prevention. Updated interim recommendations for the use of antiviral medications in the treatment and prevention of influenza for the 2009-2010 season. <http://www.cdc.gov/h1n1flu/recommendations.htm>. Accessed October 27, 2009.

Online Table C. Dosing Recommendations for Antiviral Treatment or Chemoprophylaxis of Children Younger Than 1 Year Using Oseltamivir (Tamiflu)

Age	Recommended treatment dose for 5 days	Recommended chemoprophylaxis 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 to 5 months	20 mg twice daily	20 mg once daily
6 to 11 months	25 mg twice daily	25 mg once daily

NOTE: When dispensing Tamiflu for Oral Suspension for children younger than 1 year, the oral dosing dispenser that is included in the Tamiflu package should always be removed. Pharmacists and health care personnel 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 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. When using weight-based dosing for infants younger than 1 year for treatment, those 9 months or older should receive 3.5 mg per kg per dose twice daily, and those younger than 9 months should receive 3.0 mg per kg per dose twice daily. When using weight-based dosing for infants younger than 1 year for chemoprophylaxis, those 9 months or older should receive 3.5 mg per kg per dose four times daily, and those younger than 9 months should receive 3.0 mg per kg per dose four times daily (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 personnel 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.

Adapted from Centers for Disease Control and Prevention. Updated interim recommendations for the use of antiviral medications in the treatment and prevention of influenza for the 2009-2010 season. <http://www.cdc.gov/h1n1flu/recommendations.htm>. Accessed October 27, 2009.