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Online Table A. Influenza Management Guide 2010-2011

BACKGROUND	2009 H1N1	Other Seasonal Influenza	Notes	Special Considerations for HIV-Positive Patients
Culprit viruses	**2009 H1N1, a subtype of influenza A,** also known as 2009 pandemic influenza A, novel influenza A, and swine flu	Commonly **H3N2, another subtype of influenza A** **Influenza B**	Sporadic cases of influenza have primarily been 2009 H1N1 since the 2009-2010 influenza season, although H3N2 and influenza B have had increasing incidence worldwide.	
Route of transmission	Direct contact with secretions and airborne droplets	Direct contact with secretions and airborne droplets	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: do not return to work until 24 hours after fever ends or seven days post onset of symptoms, whichever is later. Patients receiving antiviral treatment continue to be potentially infectious for four or more days after treatment initiation. Aerosol is a possible route of transmission, although limited to short distances of possibly a few feet. Surgical face masks recommended for health care personnel caring for known 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 other seasonal influenza. Probability of influenza as etiology when a patient presents with influenza-like illness: in season - approximately 80%; out of season - less than 40%.	HIV-positive patients at higher risk of influenza-related complications; course of illness might be prolonged. Additionally, 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. Vaccination of pregnant women might also provide a degree of protection for their 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: 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 5 years, especially those younger than 2 years Obese patients (BMI > 30 kg per m^2, particularly if BMI > 40) If hospitalized, patients older than 50 years with influenza have high rates of death	Adults older than 65 years	**Patients at high risk of influenza-related complications**: Age younger than 5 years, especially 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, chronic obstructive pulmonary disease], cardiovascular [excluding hypertension], renal, hepatic, conditions with increased risk of aspiration, hematologic, or metabolic [e.g., diabetes]) Immunosuppression, including HIV Persons younger than 19 years who are receiving long-term aspirin therapy (risk of Reye syndrome) Obesity (BMI > 30 kg per m^2, and particularly if BMI > 40) Cause of death is usually bacterial superinfections, most commonly staphylococcal and pneumococcal pneumonia. NOTE: Minority of patients with indications for **pneumococcal vaccination** have actually been vaccinated.	Historically, HIV-positive patients have had higher hospitalization rates, prolonged illness, and increased mortality from influenza, especially among the more immunosuppressed. **Ensure that HIV-positive patients are up to date on pneumococcal vaccinations**.
DIAGNOSIS	**2009 H1N1**	**Other Seasonal Influenza**	**Notes**	**Special Considerations for HIV-Positive Patients**
Testing	Screening test: rapid influenza diagnostic test (RIDT)—enzyme assay; sensitivity 50% to 90%; specificity 80% to 98%; test time 15 minutes or less Diagnostic tests: (a) real-time reverse transcriptase polymerase chain reaction (rRT-PCR); sensitivity and specificity 98%; test time two to four hours (b) culture (expensive); test time three to 10 days	Screening test: RIDT 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). If testing is pursued, specimens should be collected as close as possible to onset of symptoms (within first few days). Utility of RIDT is limited: low sensitivity, low specificity. False-positive results can occur when disease prevalence is low (e.g., early and late in influenza season). False-negative results can be common when disease prevalence is high (e.g., at the height of influenza season). RIDT can distinguish between influenzas A and B. Cannot distinguish between subtypes of influenza A.	
TREATMENT	**2009 H1N1**	**Other Seasonal Influenza**	**Notes**	**Special Considerations for HIV-Positive Patients**
Chemoprophylaxis NOTE: Chemoprophylaxis is generally not recommended. See Early Empiric Treatment section below.	Neuraminidase inhibitor (e.g., oseltamivir [Tamiflu]) for 10 days after last known exposure (dosing information listed in Table B)	Combination of neuraminidase inhibitor and an adamantane for 10 days after last known exposure (dosing information listed in Table B) NOTE: Because 2009 H1N1 and influenza B are resistant to adamantanes (e.g., amantadine [Symmetrel]), **do not use adamantanes** as a sole agent for chemoprophylaxis or treatment.	**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 is generally not recommended.** However, in the rare circumstance that chemoprophylaxis is being considered, it is especially not recommended if more than 48 hours have passed since last contact with an infectious person.	

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Early Empiric Treatment **Treat with neuraminidase inhibitor for five days** 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. See dosing information in Table B.	**Neuraminidase Inhibitor** options: **Oseltamivir** (Tamiflu) Dosing information below (oral pill and liquid) Approved for patients older than 1 year **Zanamivir** (Relenza) Dosing information below (inhaled powder) Approved for patients older than 7 years NOTE: Because 2009 H1N1 and influenza B are resistant to adamantanes (amantadine [Symmetrel] and rimantadine [Flumadine]), **do not use adamantanes** as a sole agent for chemoprophylaxis or treatment. In the 2009-2010 influenza season, the majority of virus was 2009 H1N1, which remained susceptible to oseltamivir. Rare sporadic resistance to oseltamivir last season usually occurred in patients previously exposed to oseltamivir. All patients were sensitive to zanamivir.	**Neuraminidase Inhibitor** options: **Oseltamivir** Dosing information below (oral pill and liquid) Approved for patients older than 1 year **Zanamivir** Dosing information below (inhaled powder) Approved for patients older than 7 years At this time, use of adamantanes is not indicated.	Most healthy patients with no risk factors for complications recover without antiviral medications. **Early empiric treatment of influenza-like illness recommended for patients at high risk of influenza-related complications.** **SPECIAL CONSIDERATIONS**: Risk of complications decreases if treated with antiviral drugs within 48 hours of symptom onset; might offer benefit after 48 hours. **Zanamivir:** can cause bronchial spasm; do not prescribe for patients with asthma or chronic lung disease. **Hospitalized patients:** treatment may be extended beyond five days for complicated illness. Some experts favor double dosage of antivirals; risks and benefits not established. **Pregnancy:** pregnant women are at high risk of complications and should receive prompt antiviral therapy. Oseltamivir and zanamivir are labeled by the U.S. Food and Drug Administration as "Pregnancy Category C" drugs. 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 with confirmed or suspected influenza. **Closed or semi-closed settings** (e.g., nursing homes and some correctional facilities): implement chemoprophylaxis if exposure to known influenza occurs. Generally does NOT include schools, camps, or workplaces where outbreaks might occur. Potential adverse effects of oseltamivir in children: nausea and vomiting; taking with food can reduce side effects. Rare reports of delirium, self-injury among children after taking neuraminidase inhibitors, which can also occur with clinical influenza.	HIV-positive patients with influenza-like illness, or who are close contacts of persons with probable or confirmed influenza, can be offered early empiric treatment versus considered for chemoprophylaxis, particularly if they are at later stages of HIV disease or with advancing immunosuppression. 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.

PREVENTION	2010-2011 Influenza Vaccine	Notes	Special Considerations for HIV-Positive Patients
Vaccines The influenza vaccine comes in a live attenuated intranasal form and an inactivated injectable form. Influenza antiviral drugs (e.g., oseltamivir or zanamivir) can interfere with immune protection from the vaccine when taken from 48 hours before through two weeks after administration of the live attenuated inhaled formulation.	The 2010-2011 influenza vaccine is a trivalent vaccine including 2009 H1N1, and seasonal variants H3N2 and influenza B Administration: One dose if 8 years or older Two doses, four or more weeks apart if 6 months to 8 years of age and did not receive at least one dose of the 2009 H1N1 vaccine plus at least one dose of the seasonal influenza vaccine previously **Do not vaccinate patients younger than 6 months** In case of vaccine shortage, Advisory Committee on Immunization Practices (ACIP) prioritizes vaccination for the following groups: 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 18 years of age BMI > 40 Nursing home residents Patients older than 50 years	Persons with moderate to severe febrile illness should not be vaccinated until symptoms abate. Most common side effect of injected vaccine is soreness at the injection site. Other adverse effects include fever, body aches, and fatigue. Most common adverse effects of nasal vaccine include rhinorrhea or nasal congestion, sore throat in adults and low-grade fever in children 2 to 6 years of age. **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, chronic lung disease, heart disease, diabetes, kidney failure, weakened immune system, or taking immunosuppressive medications. **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. Afluria, the trade name of one of the injectable formulations of the vaccine, **should not be used in children 6 months to 8 years of age** because of increased frequency of fever or febrile seizures reported among young children (mostly children younger than 5 years).	The **intranasal live attenuated** influenza vaccines are **contraindicated** for HIV-positive patients. HIV-positive patients are among the priority groups to be vaccinated. Injectable vaccine can be given at any CD4 count. NOTE: **Household contacts and health care personnel working with HIV-positive patients may receive the intranasal live attenuated vaccine.** Preferential use of the inactivated injectable vaccine is only indicated for close contacts of patients with **severe** immunocompromise who require protected environments (e.g., bone transplant units).

NOTE: *As a living document, this table was last reviewed and updated September 30, 2010. This guide will continue to be updated throughout the 2010-2011 influenza season. The latest PDF version of this table is available at http://www.nccc.ucsf.edu.*

BMI = body mass index; CDC = Centers for Disease Control and Prevention; HIV = human immunodeficiency virus.

Adapted with permission from Matin M, Goldschmidt RH. Influenza Management Guide 2010-2011.

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The NCCC's National HIV Telephone Consultation Service (Warmline) 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
Children 3 months to < 12 months†		
	3 mg per kg per dose twice daily	3 mg per kg per dose once daily
Children 0 to < 3 months‡		
	3 mg per kg per dose twice daily	Not recommended unless situation judged critical (due to limited data on use in this age group)
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

NOTE: *This table is from the following web site: http://www.cdc.gov/h1n1flu/recommendations.htm. These treatment recommendations are based on guidance previously published for the 2009-2010 influenza season. Antiviral drug treatment recommendations are not yet updated for the 2010-2011 season. This table will be revised when new information becomes available.*

**—Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available in 30-mg, 45-mg, and 75-mg capsules; and as a powder for oral suspension that is reconstituted to provide a final concentration of 12 mg per mL. If the commercially manufactured oral suspension is not available, the capsules may be opened and the contents mixed with a sweetened liquid to mask the bitter taste or a suspension can be compounded by retail pharmacies (final concentration 15 mg per mL). In patients with renal insufficiency, the dose should be adjusted based on creatinine clearance. For treatment of patients with creatinine clearance 10 to 30 mL per minute: 75 mg once daily for five days. For chemoprophylaxis of patients with creatinine clearance 10 to 30 mL per minute: 30 mg once daily or 75 mg once every other day continuing for 10 days after exposure.*

†—Weight-based dosing is preferred, however, if weight is not known, dosing by age for treatment (give two doses per day) or prophylaxis (give one dose per day) of influenza in full-term infants younger than 1 year may be necessary: 0 to 3 months (treatment only) = 12 mg (1 mL of 12 mg per mL commercial suspension); 3 to 5 months = 20 mg (1.6 mL of 12 mg per mL of commercial suspension), 6 to 11 months = 25 mg (2 mL of 12 mg per mL commercial suspension).

‡—Current weight-based dosing recommendations are NOT intended for premature infants. Premature infants may have slower clearance of oseltamivir because of immature renal function, and doses recommended for full-term infants may lead to very high drug concentrations in this age group. Limited data from a cohort of premature infants receiving an average dose of 1.7 mg per kg twice daily demonstrated drug concentrations higher than those observed with the recommended treatment dose in term infants (3 mg per kg twice daily). Observed drug concentrations were highly variable among premature infants. These data are insufficient to recommend a specific dose of oseltamivir for premature infants.

§—Zanamivir is administered by inhalation using a proprietary "Diskhaler" device distributed with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for persons with chronic respiratory diseases, such as asthma or chronic obstructive pulmonary disease, that increase the risk of bronchospasm.

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 September 30, 2010.