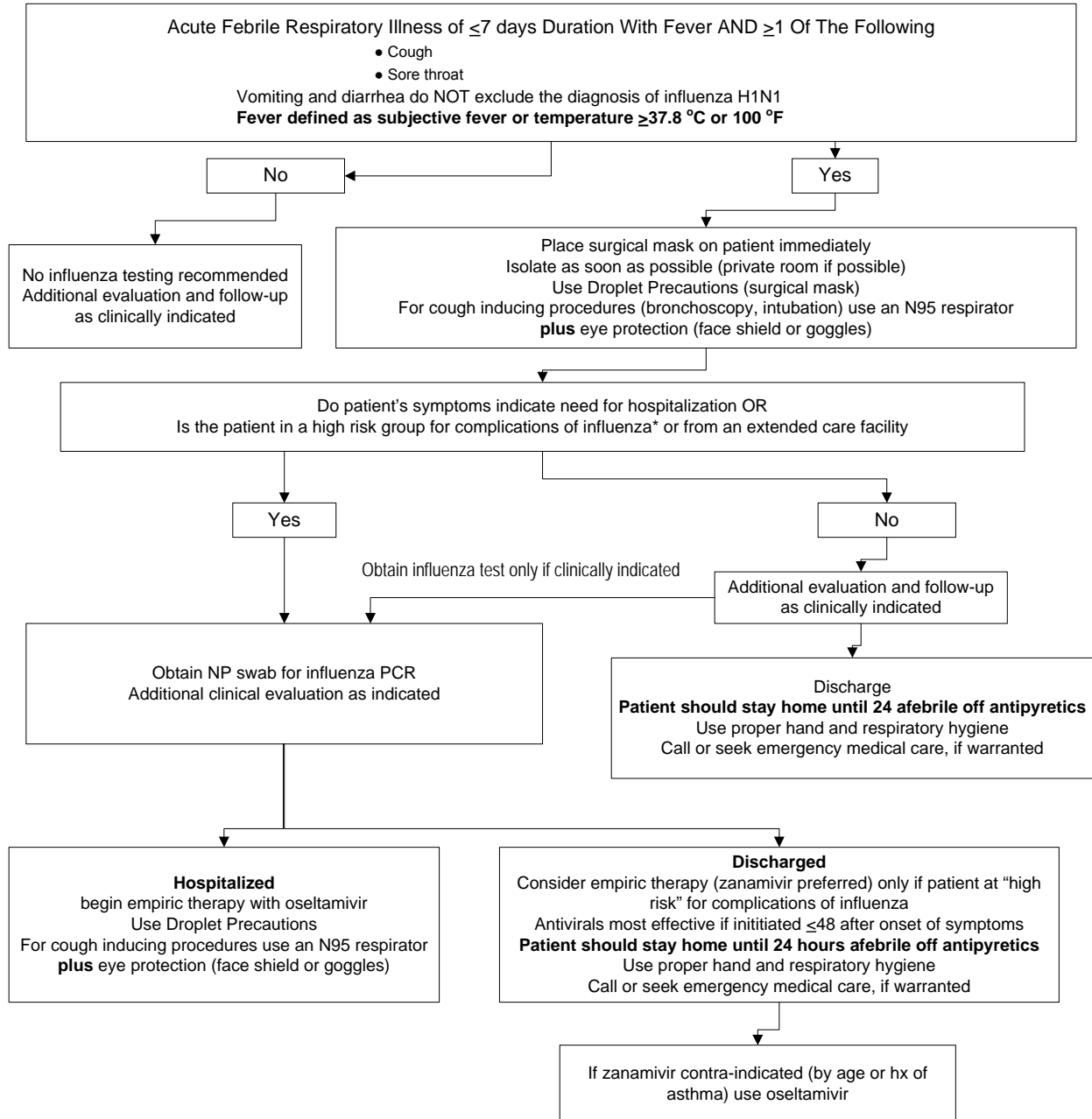


Algorithm for Evaluation of UNC Health Care Patients With Possible Novel H1N1 Influenza



* Persons considered at high risk for complications: children less than 2 years old, persons aged 65 years or older, pregnant women, persons younger than 19 years of age who are receiving long-term aspirin therapy, and persons of any age with certain chronic medical or immunosuppressive conditions (chronic pulmonary {including asthma}, cardiovascular {except hypertension}, renal, hepatic, hematological {including sickle cell disease}, metabolic disorders {including diabetes}; disorders that can compromise respiratory tract function or increase the risk of aspiration (e.g., cognitive dysfunction, seizure disorders); and immunosuppression (e.g., HIV).

Influenza (H1N1) is susceptible to oseltamivir and zanamivir but resistant to amantadine/rimantadine

Only high risk persons should be considered for post-exposure prophylaxis and therapy. Early treatment is an alternative to chemoprophylaxis after a suspected exposure.

UNC Health Care

Antiviral Dosing Recommendations for H1N1 Influenza

Treatment or prophylaxis is only recommended for persons at high risk of complications of influenza, defined as children < 2 y old, persons > 65 y, pregnant women, persons < 19 y on long-term aspirin, and persons of any age with certain chronic medical or immunosuppressive conditions (chronic pulmonary [incl. asthma], cardiovascular [except hypertension], renal, hepatic, hematologic, metabolic disorders [incl. diabetes], disorders that compromise respiratory tract function or increase the risk of aspiration [seizures, cognitive dysfunction], and immunosuppression [e.g., HIV]).

Agent, Age group		Treatment (5 days*)	Chemoprophylaxis (10 days)
Oseltamivir (Tamiflu): Preferred drug for all INPATIENTS or any patients under 5-7 years of age			
Adults		75 mg capsule twice daily	75 mg capsule once per day
Children ≥ 12 months AND ≥ 10 kg	15 kg or less	30 mg twice daily	30 mg once per day
	16-23 kg	45 mg twice daily	45 mg once per day
	24-40 kg	60 mg twice daily	60 mg once per day
	>40 kg	75 mg twice daily	75 mg once per day
Children < 12 months OR < 10 kg	< 1 week of age	2 mg/kg/dose once daily	
	≥ 1 week to < 3 months	2 mg/kg/dose twice daily Max 12 mg twice daily	Not recommended unless situation judged critical due to limited data in this age group
	3 - 5 months	2.5 to 3 mg/kg/dose twice daily Max 20 mg twice daily	2.5 to 3 mg/kg/dose once daily Max 20 mg once daily
	6 - 8 months	2.5 to 3 mg/kg/dose twice daily Max 25 mg twice daily	2.5 - 3 mg/kg/day once daily Max 25 mg once daily
	9 - 11 months	3 to 3.5 mg/kg/dose twice daily Max 30 mg twice daily	3 - 3.5 mg/kg/dose once daily Max 30 mg once daily
Zanamivir (Relenza): Preferred** drug for all OUTPATIENTS unless pre-existing airway disease (e.g., asthma) due to risk of bronchospasm or if patient is under 5-7 years of age			
Adults		Two 5-mg inhalations (10 mg total) twice per day	Two 5-mg inhalations (10 mg total) once per day
Children		<7 years Use oseltamivir	<5 years: Use oseltamivir
		≥7 years: Two 5-mg inhalations (10 mg total) twice per day	≥5 years: Two 5-mg inhalations (10 mg total) once per day (age, 5 years or older)

*If patient is admitted to an ICU, then consider extending therapy duration to 10 days in total.

**Both zanamivir (Relenza) and oseltamivir (Tamiflu) are acceptable for outpatient treatment or prophylaxis. Preferential use of Relenza in outpatients will help maintain availability of Tamiflu for pediatric patients, patients with airway disease, and inpatients.

Dosing adjustment in renal impairment:

Oseltamivir: For CrCL < 30 mL/min or GFR 10-30% of normal, adjust dosing frequency to once daily for treatment or once every other day for prophylaxis. Avoid use in renal failure.

Zanamivir: No dose adjustment is needed in renal impairment.

Dosing adjustment in hepatic impairment: None needed for either drug if mild to moderate hepatic impairment.

Product Information

Oseltamivir (Tamiflu) is available in 75 mg unit dose capsules and a 12 mg/mL; 25 mL bottle of oral suspension. The suspension is likely to be in short supply. An oral suspension can be compounded from the capsules. Alternatively, the capsules can be opened and the drug can be mixed in some chocolate syrup, orange juice, or applesauce. **We are suggesting use of the oral suspension for any doses < 75 mg. For patients receiving the 75 mg dose who cannot swallow capsules, have them open the capsules as described above.**


Zanamivir (Relenza) is available as a kit containing 1 inhaler and 5 disks. **Each dose is 2 inhalations.** Each of the disks contains 4 inhalations which equals 1 day of treatment of 2 days of prophylaxis. **The kit cannot be broken apart to dispense individual doses, so this is best for outpatient therapy.** One kit = 5 days of treatment or 10 days of prophylaxis. DO NOT use zanamivir in patients with pre-existing airway disease (e.g, asthma) due to the risk of bronchospasm.

SPECIAL POPULATIONS:

Infants Less Than 1 Year of Age

Monitoring: Apnea, hypoglycemia, renal function

The oral suspension contains sodium benzoate. This is not a contraindication for use in neonates. Benzoic acid (benzoate) is a metabolite of benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity ("gaspings syndrome") in neonates. Sodium benzoate can also displace bilirubin from protein-binding sites. Please note that the volume of drug will be small (i.e., the suspension concentration is 12 mg/mL) and the duration will be short (i.e., 5 days).

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). 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. Additional information on oseltamivir for this age group can be found at: <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.

25 September 2009