

Richard F. Daines, M.D.
CommissionerJames W. Clyne, Jr.
Executive Deputy Commissioner

November 17, 2009

To: Health Care Providers, Hospitals, Pharmacies, Nursing Homes, and Local Health Departments**From:** NYSDOH Division of Epidemiology

**HEALTH ADVISORY:
UPDATE ON INFLUENZA ANTIVIRAL MEDICATION ISSUES**

**Please distribute to staff in the Departments of Critical Care, Emergency Medicine,
Family Practice, Infection Control, Infectious Disease, Internal Medicine, Pediatrics,
Pharmacy and Pulmonary Medicine.**

The New York State Department of Health is notifying health care providers and pharmacists about several recent updates from the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) regarding antiviral medication issues for patients with suspected or confirmed influenza infection.

1. CDC's Key Messages for Clinicians on Antiviral Treatment for 2009 H1N1 Influenza

The CDC recently issued the following key messages to consider when deciding whether a patient needs to be treated with antiviral medication (from: http://www.cdc.gov/h1n1flu/antivirals/facts_clinicians.htm)

It's Not Too Late After 48 Hours

While antiviral treatment is most effective when begun within 48 hours of influenza illness onset, studies have shown that hospitalized patients still benefit when treatment is started with oseltamivir more than 48 hours after illness onset. Outpatients, particularly those with risk factors for severe illness who are not improving, might also benefit from treatment initiated more than 48 hours after illness onset.

Many 2009 H1N1 Patients Can Benefit From Antiviral Treatment

All hospitalized patients with suspected or confirmed 2009 H1N1 should receive antiviral treatment with a neuraminidase inhibitor, either oseltamivir or zanamavir. Moderately ill patients, especially those with risk factors for severe illness, and those who appear to be getting worse can also benefit from neuraminidase inhibitors.

No Risk Factors Does Not Mean No Antiviral Treatment

While antivirals are recommended for treatment of 2009 H1N1 in patients with risk factors for severe disease, some people without risk factors may also benefit from antivirals. In fact, 40% of children and 20% of adults who end up hospitalized with complications of 2009 H1N1 have no risk factors. Children and adults presenting with suspected influenza who have more serious signs or symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age. Clinical judgment is always an essential part of treatment decisions.

Treatment Shouldn't Wait Until Laboratory Confirmation

The earlier antiviral treatment is given, the more effective it is for the patient. If you suspect flu and feel antiviral treatment is warranted, then treat even if the rapid test is negative. Some rapid influenza screening tests may produce false negative results, and obtaining more accurate testing results can take more than one day.

2. Alternatives When Commercial Supplies of Tamiflu® Oral Suspension Are Limited

While commercially manufactured Tamiflu® (oseltamivir) oral suspension is the preferred product for patients who have difficulty swallowing capsules or where lower doses are needed, this product may not be locally available. Health care providers and pharmacists can consider the following alternatives when commercial supplies of Tamiflu® oral suspension are limited:

- For patients who are less than one year old, there is one alternative:
 - a suspension compounded by a retail pharmacy (see Section 3).
- For patients who are at least one year old, there are two alternatives:
 - a suspension compounded by a retail pharmacy, or
 - 30 mg, 45 mg, or 75 mg capsules, depending on the patient's weight, which may be mixed into a sweetened liquid by a caregiver, if the patient cannot swallow capsules (see Section 4).

3. Emergency Compounding of an Oral Suspension From Tamiflu® Capsules

Tamiflu® 75 mg capsules can be compounded at most retail pharmacies into a suspension when commercially manufactured Tamiflu® oral suspension, 30mg, or 45mg capsules are not available. The FDA-approved instructions for emergency compounding can be found in the DOSAGE AND ADMINISTRATION section of the Tamiflu® package insert, at:

<http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM147992.pdf>

The FDA has issued guidance to pharmacies on advance compounding of Tamiflu® oral suspension to provide for multiple prescriptions at:

<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm188629.htm>

Health care providers should be aware that the commercially manufactured Tamiflu® oral suspension concentration is **12 mg/mL**; the compounded suspension concentration is **15 mg/mL**. Thus, prescribers are advised to prescribe the dose in milligrams (mg), or to include the product name and concentration (e.g., Tamiflu® oral suspension 12mg/mL) if prescribing in milliliters (mL).

4. Mixing Tamiflu® Capsules With Sweetened Liquids

If a patient cannot swallow the Tamiflu® capsules, the 30 mg, 45 mg, or 75 mg capsules (depending on the patient's weight) can be opened and the contents mixed by a parent or caregiver with a sweetened liquid such as chocolate syrup. Questions and Answers for parents and caregivers about mixing Tamiflu® capsules with sweetened liquids can be found at:

http://www.cdc.gov/H1N1flu/antivirals/mixing_tamiflu_qa.htm

5. Tamiflu® Oral Suspension – Avoiding Potential Dosing Errors

Prescribers and pharmacists should be alert for potential dosing errors with Tamiflu® suspension; the FDA has received reports of errors where dosing instructions for the patient do not match the dosing dispenser. The dosing dispenser packaged with commercially manufactured Tamiflu® suspension has markings only in 30, 45 and 60 mg. Health care providers should write doses in mg if the dosing dispenser with the drug is in mg. Pharmacists should ensure that the units of measure on the prescription instructions match the dosing device provided with the drug. If prescription instructions specify administration using mL, the dosing device accompanying the product should be replaced with a measuring device calibrated in mL.

When dispensing Tamiflu® suspension for children younger than 1 year of age, the oral dosing dispenser that is included in the Tamiflu® suspension package should always be removed. Pharmacists and health care providers should provide an oral syringe that is capable of accurately measuring the prescribed dose in mL, and counsel the caregiver how to administer the prescribed dose. For more information, see: http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm.

6. Availability of Intravenous Peramivir

The FDA has issued an Emergency Use Authorization (EUA) to allow the use of intravenous (IV) peramivir to treat certain hospitalized adult and pediatric patients with suspected or laboratory-confirmed 2009 H1N1 virus infection. For information about the EUA and its requirements, or to electronically request peramivir from the CDC: http://www.cdc.gov/H1N1flu/EUA/peramivir_recommendations.htm

7. Availability of Intravenous Zanamivir

Limited quantities of IV zanamivir are available for compassionate use via an emergency Investigational New Drug (IND) application to the FDA. Such use may be appropriate for patients with oseltamivir-resistant influenza virus infection and when therapy with an IV agent is clinically appropriate. The medication is obtained from the manufacturer. Information about the IND process can be found at: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalsApplications/InvestigationalNewDrugINDApplication/default.htm>

Clinicians interested in enrolling patients in clinical trials of IV antiviral agents for influenza should contact the investigators of pertinent clinical trials: <http://clinicaltrials.gov/>

8. FDA Warning: Relenza® Inhalation Powder Must Not Be Nebulized

Relenza® (zanamivir) inhalation powder should only be used as directed in the prescribing information by using the Diskhaler device provided with the drug product. Relenza® inhalation powder is not intended to be reconstituted in any liquid formulation and is not recommended for use in any nebulizer or mechanical ventilator. For additional information:

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm186081.htm>

9. Additional Information on Antiviral Medications and Safety

- Centers for Disease Control and Prevention: <http://www.cdc.gov/H1N1flu/antivirals/>
- Food and Drug Administration: <http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm>