

**2008- PAHAN-0139-12-22-ADV
CDC Issues Interim Recommendations for the Use of
Influenza Antiviral Medications**

DATE: December 22, 2008
TO: Health Alert Network
FROM: Everette James
Acting Secretary of Health

**SUBJECT: CDC Issues Interim Recommendations for the Use of
Influenza Antiviral Medications**

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Due to the high prevalence of oseltamivir-resistance among influenza A (H1N1) viruses identified to date during the 2008-2009 influenza season, the Centers for Disease Control and Prevention has issued revised recommendations for the use of antiviral drugs for influenza treatment and prophylaxis. These recommendations are described in detail below.

As expected at this time of year, influenza activity is increasing in Pennsylvania, although overall activity remains low. Although only a small number of viruses have been fully examined in Pennsylvania, so far all three seasonal influenza subtypes have been identified in the Commonwealth -influenza A (H1N1) (6 isolates), influenza A (H3N2) (4 isolates) and influenza B (2 isolates). Oseltamivir-resistance has been seen among the Pennsylvania influenza A (H1N1) viruses tested. Information on influenza surveillance in Pennsylvania is available on the Pennsylvania Department of Health’s website at <http://www.dsf.health.state.pa.us/health/cwp/view.asp?a=171&q=246529>.

These findings indicate there is still abundant time to vaccinate individuals at high risk of influenza complications and those wishing to reduce their risk of influenza in the coming months. Vaccination

remains the single most effective measure to avoid influenza. The influenza A (H1N1) viruses exhibiting resistance are closely matched to the strain included in the 2008-2009 influenza vaccine.

The findings also reinforce the importance of diagnostic testing for influenza. When samples are taken, it is important to use a test that at the very least distinguishes between influenza A and B, since this will assist in decision making regarding treatment. It is also important to submit samples testing positive for influenza to reference laboratories for subtype identification. Sub typing is especially crucial in settings such as long term care facilities, health care, and other institutional settings where prophylaxis may be necessary. Such samples can be submitted to the state public health laboratory. Details concerning submission can be found at <http://www.dsf.health.state.pa.us/health/cwp/view.asp?A=167&Q=243575>

Throughout the United States, 98% of influenza A (H1N1) isolates have demonstrated oseltamivir-resistance. These H1N1 isolates remain sensitive to the other neuraminidase inhibitor, zanamivir (Relenza) and are also sensitive to the other class of influenza antiviral medications (the adamantanes rimantidine and amantadine). Adamantane drugs are not active against influenza B, and many other influenza A strains are resistant to these drugs. Therefore their use as single agents for therapy or prophylaxis should be reserved for situations where other options are unavailable.

On December 19, CDC issued the following interim recommendations regarding the use of antiviral agents. These recommendations may change as more data on antiviral resistance and circulating strains become available over the influenza season.

1. For those known to be infected with influenza B, either oseltamivir or zanamivir may be used.
2. If a patient tests positive for influenza A and the subtype is unknown, zanamivir should be used unless there are known contraindications (patient < 7 years of age, has chronic underlying airway disease, or cannot use the zanamivir inhalation device). As an alternative (or if zanamivir is unavailable), oseltamivir in combination with one of the adamantane drugs (rimantidine or amantadine) can be used.

Note the adamantane drugs (especially amantadine) are associated with balance difficulties and neuropsychiatric concerns. They should be used with caution in groups such as the elderly where balance may be an issue. Furthermore, data and experience regarding use of combination antiviral medication for influenza are limited.

3. If the patient tests positive for influenza A and the subtype is known, treatment should be based on the subtype results. For influenza A (H1N1), zanamivir could be used with oseltamivir in combination with an adamantane as the alternative recognizing the contraindications and cautions mentioned above. For influenza A (H3N2) either oseltamivir or zanamivir could be used.

4. For settings where prophylaxis may be indicating, selection of antiviral medications should be based on the resistance patterns of the virus causing disease or circulating in the community. For influenza A (H3N2) or influenza B, prophylaxis should use either oseltamivir or zanamivir. For influenza A (H1N1), prophylaxis should use zanamivir alone with rimantadine alone as an alternative.

The following chart summarizes these recommendations:

Interim recommendations for the selection of antiviral treatment using laboratory test results and viral surveillance data, United States, 2008-09 season‡

This table is an attachment to HAN issued 12/19/2008, "CDC Issues Interim Recommendations for the Use of Influenza Antiviral Medications in the Setting of Oseltamivir Resistance among Circulating Influenza A (H1N1) Viruses, 2008-09 Influenza Season"

Rapid antigen or other laboratory test	Predominant virus(es) in community	Preferred medication(s)	Alternative (combination antiviral treatment)
Not done or negative, but clinical suspicion for influenza	H1N1 or unknown	Zanamivir	Oseltamivir + Rimantadine*
Not done or negative, but clinical suspicion for influenza	H3N2 or B	Oseltamivir or Zanamivir	None
Positive A	H1N1 or unknown	Zanamivir	Oseltamivir + Rimantadine*
Positive A	H3N2 or B	Oseltamivir or Zanamivir	None
Positive B	Any	Oseltamivir or Zanamivir	None
Positive A+B**	H1N1 or unknown	Zanamivir	Oseltamivir + Rimantadine*
Positive A+B**	H3N2 or B	Oseltamivir or Zanamivir	None

*Amantadine can be substituted for rimantadine but has increased risk of adverse events. Human data are lacking to support the benefits of combination antiviral treatment of influenza; however, these interim recommendations are intended to assist clinicians treating patients who might be infected with oseltamivir-resistant influenza A (H1N1) virus.

**Positive A+B indicates a rapid antigen test that cannot distinguish between influenza and influenza B viruses

‡ Influenza antiviral medications used for treatment are most beneficial when initiated within the first two days of illness. Clinicians should consult the package insert of each antiviral medication for specific dosing information, approved indications and ages, contraindications/warnings/precautions, and adverse effects.

"The full-text of the CDC Health Advisory released on Friday, December 19, 2008 (CDCHAN-00279-2008-12-19-ADV-N; *CDC Issues Interim Recommendations for the Use of Influenza Antiviral Medications in the Setting of Oseltamivir Resistance among Circulating Influenza A (H1N1) Viruses, 2008-09 Influenza Season*) is accessible at <http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00279>."

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This information is current as of December 22, 2008, but may be modified in the future. We will continue to post updated information regarding the most common questions about this subject.