Criteria for Use of Antiviral Agents for Influenza

VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.

Three licensed influenza antiviral agents are generally available in the United States (U.S.): amantadine, rimantadine, and oseltamivir. (A fourth, zanamivir [Relenza™], is licensed by FDA but not widely available.) The first three are approved for treatment and prevention of influenza in certain situations AND are on the VA National Formulary.

Chemoprophylaxis for seasonal influenza

Historically, amantadine and rimantadine have been 70-90% effective in preventing illness from influenza A infection (not active against influenza B). However, recent reports have shown increasing resistance to adamantanes, and for the 2005-06 influenza season, 91% of the influenza A (H3N2) isolates tested by the CDC demonstrate resistance to amantadine and rimantadine.

Based on this information, the CDC (and the VA) recommends that oseltamivir be used for chemoprophylaxis for the 2005-2006 season and that neither amantadine nor rimantadine be used for chemoprophylaxis this season.

Table 1: Criteria for chemoprophylaxis with oseltamivir for seasonal influenza

Patient falls into a high risk group* for serious complications from influenza AND there is seasonal influenza in the community or an institutional outbreak

AND ≥ 1 of the following:

- Resident of a nursing home, hospital, etc. where there has been an institutional outbreak of influenza (provide chemoprophylaxis , for the duration of the outbreak regardless of prior vaccination)
- Patient has not had time to mount an immune response to the vaccine (provide chemoprophylaxis for a period of 2 weeks after vaccination)
- Patient does not receive, cannot receive or does not respond to vaccine (i.e., immunocompromised patients (provide chemoprophylaxis for duration of outbreak, i.e., 6 – 8 weeks)

OR

Patient is a healthcare worker** AND there is seasonal influenza in the community or an institutional outbreak

AND ≥ 1 of the following:

- Regardless of prior vaccination: works in an institution (nursing home, hospitals, etc.) where there has been an outbreak of influenza (provide chemoprophylaxis for the duration of the outbreak)
- Has direct patient care responsibilities and is not able to obtain influenza vaccine. (provide chemoprophylaxis for duration of outbreak, i.e., 6 – 8 weeks)

*High-risk patients include: > 65years old, nursing home patient or resident of VA long term care facility, chronic diseases (e.g. heart disease, lung disease, diabetes, blood diseases, end-stage renal disease, cancer or cancer treatment, HIV/AIDS, steroid therapy, persons who are or intend to become pregnant during the influenza season – through Spring 2006. Persons who are or intend to become pregnant should consult their primary healthcare providers. Because of the unknown effects of influenza antiviral drugs on

pregnant women and their fetuses, these drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

**Chemoprophylaxis of healthcare works should be prescribed in consultation with occupational health

Table 2: Dosing for influenza prophylaxis

		13-64 years old	≥ 65 years old	Hepatic or renal dysfunction
Oseltamivir	Influenza A or B	75mg once daily	75mg once daily	CrCl < 30 ml/min: 75 mg every other day

Treatment for Seasonal Influenza

Oseltamivir is indicated for treatment of Influenza A and B based on the following criteria. ** The CDC also recommends the use of zanamavir (which is not currently on the VA National Formulary) for treatment of influenza for the 2005-06 season.

Table 3: Criteria for treatment with oseltamivir for seasonal influenza

Patients who already have serious cases of influenza (e.g., warranting hospitalization)

OR

Onset of symptoms is within 48 hours AND Patient is at risk for a potentially life-threatening influenza-related illness*

The following patients should be prioritized to receive oseltamivir if supplies are limited

Patients who already have serious cases of influenza (e.g., warranting hospitalization)

OR

Onset of symptoms is within 48 hours AND Patient is at risk for a potentially life-threatening influenza-related illness*

*High-risk patients include: > 65years old, nursing home patient, chronic diseases (e.g. heart disease, lung disease, diabetes, blood diseases, end-stage renal disease, cancer or cancer treatment, HIV/AIDS, steroid therapy

** The most reliable way to diagnose influenza is by the use of specific laboratory tests (http://www.cdc.gov/flu/professionals/diagnosis/). Where accurate, rapid testing is not available, clinicians need to rely upon epidemiological data and clinical findings. However, while clinical criteria, i.e., the presence of fever and cough has been reported to have an accuracy as high as 80 – 90% in otherwise health young adults[1-3], the predictive value of such symptom complex is significantly less in older adults[4], children[5] and nursing home residents[6,7].

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Table 4: Dosing for treatment of influenza

		13-64 years old	≥ 65 years old	Hepatic or renal dysfunction
Oseltamivir	Influenza A or B	75mg twice daily for 5 days	75mg twice daily for 5 days	CrCl 10-30ml/min 75mg once daily for 5 days. No recommendations are available for patients undergoing hemodialysis or continuous peritoneal dialysis. Oseltamivir has not been studied in patients with liver disease.
Zanamivir¶	Influenza A or B	10mg (2 inhalations) twice daily	10mg twice daily	No dosage reduction is recommended for patients with mild-moderate renal impairment Zanamivir has not been studied in patients with liver disease.

¶Zanamivir is available as a dry powder inhaler that is orally inhaled. Doses are packaged in a blister pack and must be loaded into the Rotadisk. Each blister contains 5mg of drug.

Adverse events of oseltamivir and zanamivir

Oseltamivir: Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment (nausea without vomiting, approximately 10%; vomiting, approximately 9%) than among persons receiving placebo (nausea without vomiting, approximately 6%; vomiting, approximately 3%).

Zanamivir: 13% of patients receiving zanamivir and 14% of patients who received placebo (inhaled powdered lactose vehicle) experienced a >20% decline in forced expiratory volume in 1 second (FEV1) after treatment. Because of the risk for serious adverse events and because the efficacy has not been demonstrated among this population, zanamivir is not generally recommended for treatment for patients with underlying airway disease. However, if benefits outweigh the risk, and zanamivir is used in patients with asthma or COPD, a fast-acting bronchodilator should be available when inhaling zanamivir.

The PBM-MAP acknowledges Larry Mole, PharmD Director of VA Center for Quality Management in Public Health and Pam Belperio, PharmD, BCPS National Public Health Clinical Pharmacist, VA Center for Quality Management in Public Health for their participation in the development of the criteria.