INTRODUCTION
The use of antiviral medications for management of influenza is an important component of a multi-faceted response to an influenza pandemic. Treatment with a class of agents called neuraminidase inhibitors has been shown to decrease severe complications of influenza, such as pneumonia and to reduce hospitalizations. Antiviral usage may be particularly important before vaccine is available and for those for whom vaccination may be medically contraindicated. The effect of antiviral medications is usually immediate and does not interfere with the response to inactivated influenza vaccines. It is also essential to avoid inappropriate use of antiviral medications because that may lead to influenza virus developing resistance to these medications. Ultimately, vaccination against the pandemic influenza virus is likely to provide the most durable protection against the illness but pandemic vaccine may not be available in a timely manner.

Antiviral medications for treatment of influenza included in the Strategic National Stockpile (SNS) include the neuraminidase inhibitors, oseltamivir (Tamiflu®) and zanamivir (Relenza®). The Centers for Disease Control and Prevention (CDC) also has added Peramivir for intravenous administration for patients who have severe, complicated or progressive illness or who are hospitalized or who are unable to take oral medication or in whom oral medication appears to be ineffective.

OBJECTIVES
- Describe plan for allocation, distribution, and administration of antiviral medications.
- Monitor antiviral medication use and safety during a pandemic.

PLANNING ASSUMPTIONS
- Missouri Department of Health and Senior Services (DHSS) will continue to follow the guidance issued by the CDC regarding the use of antiviral medications. (Please see specific references in the resources section at the end of this annex.)
- Treatment with a neuraminidase inhibitor (oseltamivir [Tamiflu®] or zanamivir [Relenza®]) will be effective in decreasing risk of pneumonia, will decrease hospitalization by about half (as shown for interpandemic influenza) and will also decrease mortality.
- The effectiveness of antiviral medications against a new pandemic influenza strain cannot be completely predicted.
- The choice of particular antiviral medications will depend on what is known about the viral resistance pattern at the time of pandemic and the availability of a particular drug.
- Antiviral resistance to the adamantanes (amantadine and rimantadine) may limit their use during a pandemic.
- Early treatment is a more efficient use of antiviral medications than prophylaxis.
- Early treatment after the onset of disease is most effective in decreasing the risk of complications and shortening illness duration. Generally, treatment should be given within the first 48 hours.
Antiviral use will be most important during the time when vaccine isn’t yet available, when supply of new vaccine is limited, and while immunity from the vaccine is being developed.

Within local communities, private providers, health care, industry and others may have purchased antiviral medication caches for protection of their workers.

**EMERGENCY USE AUTHORIZATION (EUA)**

Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act), amended by the Project BioShield Act of 2004, permits authorization of such products for use in diagnosing, treating or preventing serious or life-threatening diseases or conditions caused by biological, chemical, radiological or nuclear agents, if certain statutory criteria are met.

Should a pandemic occur, Missouri would follow the guidance and requirements issued by the federal government related to use of antiviral medications. It is anticipated the Secretary would declare a public health emergency therefore the Federal Drug Administration (FDA) has authority to issue an Emergency Use Authorization (EUA) for emergency use of Tamiflu® (oseltamivir) and Relenza® (zanamivir). More information on the EUA can be found at http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm.

In addition to the medical countermeasures supplied by the SNS, Tamiflu® and Relenza® that are supplied via state and local governments are also covered by the EUA, if the terms and conditions of the EUA are met.

**PUBLIC READINESS AND EMERGENCY PREPAREDNESS (PREP) ACT**

The PREP Act authorizes the Secretary of the Department of Health and Human Services (Secretary) to issue a declaration (PREP Act declaration) that provides immunity from tort liability (except for willful misconduct) for claims of loss caused, arising out of, relating to or resulting from administration or use of countermeasures to diseases, threats and conditions determined by the Secretary to constitute a present or credible risk of a future public health emergency to entities and individuals involved in the development, manufacture, testing, distribution, administration and use of such countermeasures.

A PREP Act declaration is specifically for the purpose of providing immunity from tort liability, and is different from, and not dependent on, other emergency declarations. The PREP Act also authorizes an emergency fund in the United States Treasury to provide compensation for injuries directly caused by administration or use of a countermeasure covered by the Secretary’s declaration. While no funds have been appropriated for this purpose, if funds are appropriated, compensation may then be available for medical benefits, lost wages and death benefits to individuals for specified injuries.

The existing PREP Act declarations were amended in Spring 2009 to include H1N1.
DISTRIBUTION OF ANTIVIRAL MEDICATIONS IN MISSOURI

- Antiviral medications purchased with publicly funded monies through the SNS are to be used for treatment only.
- The model of delivery will vary in local communities depending on each jurisdiction’s plan and resources.
- In general, antiviral medications will be delivered to pre-determined sites, such as local health departments, hospitals, and pharmacies.
- The amounts that will be delivered to the sites will be determined by the community’s population size.
- Portion of antiviral medications will be pre-positioned within the State for easy access when needed.
- The Missouri Department of Health and Senior Services (DHSS) continues to work closely with local public health agencies (LPHAs) to enhance specific distribution plans of these assets for communities utilizing available health care providers and resources.

As part of antiviral medication planning with LPHAs, the state of Missouri has pre-positioned a portion of the SNS allocation of antiviral medications. These assets include limited amounts of Tamiflu tablets (30mg; 45mg; 75mg). A limited number of Relenza Diskhalers were pre-positioned as well.

LPHAs will utilize the SNS Missouri Health Strategic Architectures and Information Cooperative (SNS MOHSAIC) system for ordering antiviral medications from the SNS stockpile. LPHAs will work closely with community partners to integrate plans for antiviral distribution into existing pandemic influenza plans and identify the best method of distribution and dispensing for their population.

LPHAs will identify community partners who can prescribe antiviral medications for treatment and who would be willing to dispense this medication and comply with other stipulations set forth by DHSS and CDC regarding the distribution of subsidized medications. Community partners could include hospital pharmacies, retail pharmacies, health care providers, Federally Qualified Health Centers and other facilities with appropriate storage facilities, hours of operation and staff to dispense the medication.

USING ANTIVIRAL MEDICATIONS TO TREAT HIGH-RISK INDIVIDUALS

The CDC is strongly encouraging state health departments to use assets provided by the states and the SNS for treatment of high-risk individuals. These individuals may not have routine access to medications through commercial pharmacy distribution systems and may be unable to purchase antiviral medications prescribed to them. High-risk individuals are defined as having increased risk of developing severe disease or complications from influenza. The high-risk groups include:
• Pregnant women.
• Individuals with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic hematological (including sickle cell disease), neurologic, neuromuscular or metabolic disorders (including diabetes mellitus).
• Individuals with immunosuppression, including that caused by medications or by HIV.
• People younger than 19 years of age who are receiving long-term aspirin therapy.
• Children younger than 5 years old. The risk of severe complications from influenza is highest among children younger than 2 years old.
• Adults 65 or older.

It is likely that current antiviral usage guidelines including high risk groups and prioritization recommendations will change when epidemiologic data on a specific pandemic virus becomes available or when supplies of antiviral medications are greatly increased.

Many communities have hospitals or clinic pharmacies that provide direct dispensing of medications or onsite prescription assistance programs for treatment of high-risk individuals that may not otherwise have affordable access. A broad, forward deployment of antiviral medications to these locations can help ensure that underinsured or uninsured high-risk individuals with influenza will be able to receive antiviral medications for treatment.

A forward deployment also can help ensure rapid dispensing of medication to those who might otherwise have limited or no access for obtaining medications through commercial pharmacies.

DHSS has provided consultation and training to LPHAs and their partners regarding antiviral security measures.

ANTIVIRAL MEDICATIONS ADVERSE EVENTS
For information on recognizing adverse events (side effects) related with use of each medical countermeasure, please refer to the respective EUA Fact Sheets for that product. Health care professionals and consumers may report serious adverse events (side effects) with the use of these products or product quality problems to the FDA's MedWatch Adverse Event Reporting program.

FDA’s MedWatch can be reached:
Online: FDA's MedWatch Adverse Event Reporting program at https://www.accessdata.fda.gov/scripts/medwatch/
Regular Mail: Use postage-paid FDA form 3500 and mail to:
MedWatch
5600 Fishers Lane
Rockville, MD 20852-9787
Fax: (800) FDA-0178
Phone: (800) FDA-1088

Additionally, questions related to adverse reactions may be directed to the DHSS, Department Situation Room (DSR) by calling 1-800-392-0272.
During the 2009-2010 influenza season an H1N1 information line (24 hour/day, seven
days/week) was activated to provide information as well as answer calls regarding potential
adverse reactions.
RESOURCES

*Department of Health and Human Services Pandemic Plan*
http://www.hhs.gov/pandemicflu/plan

Food and Drug Administration
http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm

*Updated Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza*
http://www.cdc.gov/flu/

*Recommendations of the Advisory Committee on Immunization Practices (ACIP): Information for Health Care Professionals*
http://www.cdc.gov/flu/professionals/antivirals/

Missouri Department of Health and Senior Services
http://health.mo.gov/emergencies/panflu/pangen.php