Health Update:

2009 H1N1 Influenza Update 13: Antiviral Treatment of Hospitalized Patients, Peramivir EUA, New CDC Clinical Support Line, Reporting Selected Categories of Influenza Patients, Influenza Vaccinations and Pregnant Women

October 29, 2009

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Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies or the public.

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Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

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Health Update
October 29, 2009

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SUBJECT: **2009 H1N1 Influenza Update 13: Antiviral Treatment of Hospitalized Patients, Peramivir EUA, New CDC Clinical Support Line, Reporting Selected Categories of Influenza Patients, Influenza Vaccinations and Pregnant Women**

This Health Update provides information on: 1) antiviral treatment options for hospitalized influenza patients; 2) Emergency Use Authorization (EUA) of peramivir; 3) a new CDC clinical support line for medical providers caring for pregnant/postpartum women; 4) reporting selected categories of influenza patients; 5) influenza vaccinations and pregnant women.

Antiviral Treatment Options for Hospitalized Patients with Suspected or Confirmed Influenza

The Centers for Disease Control and Prevention (CDC) has issued updated antiviral treatment options for hospitalized influenza patients utilizing the neuraminidase inhibitors (NAIs) oseltamivir, zanamivir, and peramivir. (The Food and Drug Administration [FDA] has recently issued an Emergency Use Authorization [EUA] to allow the use of peramivir to treat certain adult and pediatric patients with suspected or confirmed 2009 H1N1 influenza. See the next section for additional information on peramivir and the EUA.) The updated antiviral treatment options for hospitalized patients are available from CDC at http://www.cdc.gov/H1N1flu/EUA/peramivir_recommendations.htm. Key points include the following:

- Early treatment with oseltamivir has been associated with survival in hospitalized and critically ill patients with 2009 H1N1 influenza virus infection.
- Empiric antiviral treatment with oral oseltamivir or orally inhaled zanamivir should be administered as soon as possible for all persons with suspected or confirmed influenza requiring hospitalization. Initiation of antiviral treatment should not be delayed pending laboratory confirmation of influenza.
- Intravenous (IV) peramivir has been authorized for use by FDA, subject to the EUA terms and conditions.
- IV peramivir may be appropriate for certain hospitalized and critically ill patients with suspected or confirmed 2009 H1N1 influenza, such as patients not responding to either an oral or inhaled antiviral therapy and patients without a dependable oral or inhaled route of drug delivery (e.g. patients unable or unlikely to absorb oseltamivir due to ileus or high nasogastric tube output).
- Clinicians should carefully review the health care provider fact sheet on peramivir, (http://www.cdc.gov/h1n1flu/eua/Final%20HCP%20Fact%20sheet%20Peramivir%20IV_CDC.pdf). This fact sheet also includes the terms and conditions of the EUA, and safety and efficacy data on peramivir.
- To request IV peramivir (licensed clinicians with prescribing privileges ONLY), go to http://emergency.cdc.gov/h1n1antivirals/. For any questions, call 1-800-CDC-INFO (1-800-232-4636), 24 hours a day, 7 days a week.

Emergency Use Authorization (EUA) of Peramivir

Currently there are no FDA-approved IV antiviral products for the treatment of hospitalized patients with influenza. Peramivir is an investigational NAI available in IV formulation, whose efficacy and safety have not yet been established. FDA has recently issued an EUA to allow the use of peramivir to treat certain adult and pediatric patients with suspected or laboratory-confirmed 2009 H1N1 influenza. The following provides brief summary information on the use of peramivir under the EUA. For more comprehensive information, go to http://www.cdc.gov/h1n1flu/eua/peramivir.htm.

Peramivir is authorized for the following patients who are admitted to a hospital:

- Adult patients for whom therapy with an IV agent is clinically appropriate, based upon one or more of the following reasons:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible, or
  - the clinician judges IV therapy is appropriate due to other circumstances
- Pediatric patients for whom an IV agent is clinically appropriate because:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible

Do not use IV peramivir for the treatment of seasonal influenza A or B virus infections, for outpatients with acute uncomplicated 2009 H1N1 virus infection, or for pre- or post-exposure chemoprophylaxis (prevention) of influenza.

Clinical judgment is an important factor in determining which hospitalized or critically ill patients would benefit from IV peramivir. If peramivir is ordered, hospitalized patients should continue to receive therapy with an available NAI (oseltamivir or zanamivir) until after the first dose of peramivir has been administered. Combined therapy with oseltamivir or zanamivir and peramivir is not recommended because of their overlapping mechanism of action.

The standard adult dose of peramivir is 600 mg once a day, administered IV for 5 to 10 days. The decision to administer peramivir treatment longer than 5 days should be based upon clinical judgment and virological data (rRT-PCR or viral culture), if available.

Commonly reported adverse events in peramivir clinical trials were diarrhea, nausea, vomiting, and neutropenia. Additional adverse events associated with the drug, some of which may be serious, may become apparent with more widespread use.

Clinicians considering the use of peramivir under the EUA must read and understand the content of the provider fact sheet (http://www.cdc.gov/h1n1flu/eua/Final%20HCP%20Fact%20sheet%20Peramivir%20IV_CDC.pdf) and the terms and conditions on the EUA prior to initiating a request for this product. The fact sheet also contains the limited available safety and efficacy data, as well as dosing information, including the recommended dose with renal insufficiency.

If medical providers, after reviewing materials available at http://www.cdc.gov/h1n1flu/eua/peramivir.htm, have clinical questions relating to the use of IV peramivir, they should contact CDC INFO at 1-800-232-4636, 24 hours a day, 7 days a week. (For TTY, call 1-888-232-6348.)

To request IV peramivir, clinicians should go to http://emergency.cdc.gov/h1n1antivirals/.

(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/].)

(Note on IV zanamivir: IV zanamivir is available for compassionate use from its manufacturer via an emergency Investigational New Drug (IND) application to FDA. Go to FDA's IND Application Web site at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm.)

CDC Clinical Support Line for Medical Providers Caring for Pregnant/Postpartum Women

CDC has established a new clinical support line to provide technical assistance to medical providers caring for seriously ill pregnant or immediately postpartum (within 6 weeks of delivery) women with influenza. The telephone number is 404-368-2133. Clinical support is available from board-certified OB/GYN subject matter experts 24 hours a day, 7 days a week. Note that this number should only be used for consultation on seriously ill pregnant or postpartum patients, or to report seriously ill pregnant or immediately postpartum patients who are admitted to an intensive care unit (ICU) or who die (see the next section). For questions regarding pregnant women who are not seriously ill, providers can call 1-800-232-4636.

Reporting Selected Categories of Influenza Patients

The following influenza cases should be reported directly to CDC:

1. Any pregnant or immediately postpartum (within 6 weeks of delivery) woman with severe influenza (2009 H1N1 or seasonal) who is either: a) admitted to an ICU, or b) dies. The report should be made by calling 404-368-2133, or by completing the case report form available at http://www.dhss.mo.gov/BT_Response/SwineFlu/PregnantandPostPartumWomen.pdf and faxing it to 404-248-4094.

2. Any patient with 2009 H1N1 influenza virus infection suspected of having hemorrhagic pneumonitis syndrome (HPS). Suspected HPS can be considered in a patient with all of the following:
   - Confirmed 2009 H1N1 virus infection, and
   - Clinical or radiographic evidence of pneumonia, and
   - Acute onset of illness accompanied by dyspnea and hemoptysis, and
   - Severe respiratory illness requiring mechanical ventilation or resulting in death

   OR
   - Confirmed H1N1 virus infection, and
   - A bronchoalveolar lavage (BAL) specimen with hemorrhagic fluid, or hemosiderin laden macrophages on Prussian blue staining

   The report should be made by completing the HPS case report form, which is available at http://www.dhss.mo.gov/BT_Response/SwineFlu/HPS.pdf, and faxing pages 2-7 to 404-639-3866 (ATTN: Erin Kennedy).

All influenza-associated pediatric deaths (≤18 years of age) should be reported within one day to the local public health agency, or to the Missouri Department of Health and Senior Services (DHSS) at 573-751-6113 or 800-392-0272. For all suspected or confirmed influenza-associated pediatric deaths, a DHSS disease case report (CD-1) form (http://www.dhss.mo.gov/CommunicableDisease/CD-1.pdf) should be completed. In addition, for all confirmed influenza-associated pediatric deaths, a separate CDC influenza-associated pediatric death report form (http://www.dhss.mo.gov/CDManual/PedDeathform.pdf) should also be completed.

Influenza Vaccinations and Pregnant Women

The following is from an October 22, 2009, press release from the American Medical Association (AMA), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG).

To help stress the urgent message that pregnant women must get vaccinated against both seasonal influenza and 2009 H1N1 to protect themselves and their unborn baby, the AMA, AAFP, ACOG, and CDC joined forces today. In a group letter sent to health care professionals nationwide, leaders from the four groups emphasized the increased number of deaths among pregnant women from influenza and provided helpful information for medical professionals.

The letter urges health care professionals to vaccinate their pregnant patients and counsel them on the benefits of the vaccine. Both the seasonal influenza vaccine and the H1N1 vaccine are safe to administer to pregnant women in any trimester and can be given simultaneously. Pregnant women should be given the flu shot, not the nasal spray version of the vaccine.

[See the letter at http://www.acog.org/departments/resourceCenter/2009H1N1JointDearColleagueLtr.pdf.]

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).