MISSISSIPPI STATE DEPARTMENT OF HEALTH

This is an official
MS Health Alert Network (HAN) Advisory

MESSAGE ID: **MSHAN-20171228-00409-ADV (Health Advisory)**

RECIPIENTS: **All Physicians, Hospitals, ERs, ICPs, NPs, and Healthcare Providers - Statewide**

DATE: **Thursday, December 28, 2017**

SUBJECT: **Recent Increased Influenza Activity and Nursing Home Outbreaks**

Key Messages:

- Influenza activity has increased recently in both Mississippi and the US; the recent increase in influenza activity in Mississippi exceeds an earlier peak of activity seen in November 2017;
- **Nursing homes have been increasingly impacted in Mississippi this season, with a marked increase in the number of reported outbreaks in the last two weeks. Of the 45 reported outbreaks in long-term care facilities this season to date; 26 (58%) have occurred since December 14, 2017;**
- Influenza A H3N2 is the predominant strain in the US. While earlier in the season influenza A H1N1 was the predominant strain in Mississippi, the majority of specimens testing positive at the Mississippi Public Health Laboratory are now H3N2;
- Seasons predominated by H3N2 are associated with increased hospitalizations and deaths in individuals ≥65 years of age and in young children;
- Vaccine effectiveness (VE) against H3N2 is estimated by the Centers for Disease Control and Prevention (CDC) to be similar to last season when VE was only 32%;
- **Due to the potential impact on the elderly and nursing home residents, young children and those at higher risk of complications, early recognition and treatment of influenza with neuraminidase inhibitor (NAI) antiviral medications is especially important.** Clinicians are advised to treat all hospitalized patients and all high-risk patients with suspected influenza (inpatient or outpatient) as soon as possible to reduce the risk of complications.
- Clinicians should be aware that a negative rapid influenza diagnostic test result does not exclude a diagnosis of influenza in a patient with suspected influenza when there is influenza activity in the community.
- **Influenza vaccine is still recommended for unvaccinated persons and can prevent hospitalizations and deaths even when there is reduced vaccine effectiveness;**
- The CDC issued a Health Alert Message that discusses recommendations for antiviral treatment of patients with influenza this season, of which an excerpt is attached below. The complete message may be reviewed at https://emergency.cdc.gov/han/han00409.asp
- To report outbreaks or if you have questions please call the MSDH Office of Epidemiology at 601-576-7725 (601-576-7400 after hours, holidays, and weekends).

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The Mississippi State Department of Health (MSDH) is asking providers to:

- Suspect influenza when evaluating patients with a febrile respiratory disease;
- Treat all hospitalized patients and all high-risk patients (either hospitalized or outpatient) with suspected influenza as soon as possible with a neuraminidase inhibitor antiviral. While antiviral drugs work best when treatment is started within 2 days of illness onset, clinical benefit has been observed even when treatment is initiated later. **Decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza.** High risk individuals include:
    - Hospitalized patients,
    - Children younger than 5 years, especially those younger than 2 years,
    - Adults 65 years and older,
    - Pregnant women,
    - Residents of nursing homes or other chronic-care facilities. MSDH also recommends that all non-ill residents receive prophylactic antivirals when an influenza outbreak is identified in a nursing home setting (see resources for recommendations around influenza in long-term care settings),
    - Persons with underlying chronic medical problems such as pulmonary disease, cardiovascular disease, diabetes and obesity, among others;
- Continue to recommend influenza vaccine for all unvaccinated persons, especially staff and residents in healthcare settings or those at higher risk for complications.
- To report outbreaks or if you have questions please call the MSDH Office of Epidemiology at 601-576-7725 (601-576-7400 after hours, holidays, and weekends).

Regards,

Paul Byers, MD
State Epidemiologist

Resources

- Interim Guidance for Influenza Outbreak Management in Long-Term Care Facilities: http://www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm
- Mississippi influenza surveillance weekly reports: http://www.healthyms.com/msdhsite/_static/14,0,199,777.html
- Summary of Influenza Antiviral Treatment Recommendations for Clinicians: http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

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(The following is an excerpted version of the original CDC Health Advisory—the full advisory may be obtained at https://emergency.cdc.gov/han/han00409.asp)

This is an official

CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
December 27, 2017, 1030ET (10:30 AM ET)
CDC HAN-00409

Seasonal Influenza A (H3N2) Activity and Antiviral Treatment of Patients with Influenza

Summary

The Centers for Disease Control and Prevention (CDC) is providing: 1) a notice about increased influenza A(H3N2) activity and its clinical implications; 2) a summary of influenza antiviral drug treatment recommendations; 3) an update about approved treatment drugs and supply this season; and 4) background information for patients about influenza treatment.

Background

In the United States (U.S.), influenza activity has increased significantly over recent weeks with influenza A(H3N2) viruses predominating so far this season. In the past, A(H3N2) virus-predominant influenza seasons have been associated with more hospitalizations and deaths in persons aged 65 years and older and young children compared to other age groups. In addition, influenza vaccine effectiveness (VE) in general has been lower against A(H3N2) viruses than against influenza A(H1N1)pdm09 or influenza B viruses. Last season, VE against circulating influenza A(H3N2) viruses was estimated to be 32% in the U.S. CDC expects that VE could be similar this season, should the same A(H3N2) viruses continue to predominate. For this reason, in addition to influenza vaccination for prevention of influenza, the use of antiviral medications for treatment of influenza becomes even more important than usual. The neuraminidase inhibitor (NAI) antiviral medications are most effective in treating influenza and reducing complications when treatment is started early. Evidence from previous influenza seasons suggests that NAI antivirals are underutilized in outpatients and hospitalized patients with influenza who are recommended for treatment.

This CDC Health Advisory is being issued to—

1) Remind clinicians that influenza should be high on their list of possible diagnoses for ill patients because influenza activity is increasing nationwide, and

2) Advise clinicians that all hospitalized patients and all high-risk patients (either hospitalized or outpatient) with suspected influenza should be treated as soon as possible with a neuraminidase inhibitor antiviral. While antiviral drugs work best when treatment is started within 2 days of illness onset, clinical benefit has been observed even when treatment is initiated later.

Recommendations

CDC Antiviral Recommendations for the 2017–2018 Season

CDC recommends antiviral medications for treatment of influenza as an important adjunct to annual influenza vaccination. Treatment with neuraminidase inhibitors has been shown to have clinical and public health benefit in reducing illness and severe outcomes of influenza based on evidence from randomized controlled trials, meta-analyses of randomized controlled trials, and observational studies during past influenza seasons and during the 2009 H1N1 pandemic.

All Hospitalized, Severely Ill, and High-Risk Patients with Suspected or Confirmed Influenza Should Be Treated with Antivirals

Any patient with suspected or confirmed influenza in the following categories should be treated as soon as possible with a neuraminidase inhibitor:

1) Any patient who is hospitalized—treatment is recommended for all hospitalized patients;
2) Any patient who has severe, complicated, or progressive illness—this may include outpatients with severe or prolonged progressive symptoms or who develop complications such as pneumonia but who are not hospitalized;
3) Any patient who is at higher risk for influenza complications but not hospitalized. Patients in this group include—

- children younger than 2 years (although all children younger than 5 years are considered at higher risk for complications from influenza, the highest risk is for those younger than 2 years)
- adults aged 65 years and older
- persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)
- people with immunosuppression, including that caused by medications or by HIV infection
- women who are pregnant or postpartum (within 2 weeks after delivery)
- people aged younger than 19 years who are receiving long-term aspirin therapy
- American Indians/Alaska Natives
- people with extreme obesity (i.e., body-mass index is equal to or greater than 40)
- residents of nursing homes and other chronic-care facilities

Timing of Treatment and Implications for Patient Evaluation, Treatment, and Testing

Clinical benefit is greatest when antiviral treatment is administered as early as possible after illness onset. Therefore, antiviral treatment should be started as soon as possible after illness onset and **should not be delayed** even for a few hours to wait for the results of testing. Ideally, treatment should be initiated within 48 hours of symptom onset. **However, antiviral treatment initiated later than 48 hours after illness onset can still be beneficial for some patients.**

A very large observational study of more than 29,000 hospitalized influenza patients reported that while the greatest clinical benefit was found when antiviral treatment was initiated within 48 hours of illness onset, starting antiviral treatment more than 2 days after onset had survival benefit in adults versus no treatment. Also, a randomized, placebo-controlled study suggested clinical benefit when oseltamivir was initiated 72 hours after illness onset among febrile children with uncomplicated influenza.[vii] Clinical judgment, on the basis of the patient's disease severity and progression, age, underlying medical conditions, likelihood of influenza, and time since onset of symptoms, is important when making antiviral treatment decisions for outpatients, particularly those who are not at increased risk for influenza complications.

Because of the importance of early treatment, **decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza**. Therefore, empiric antiviral treatment should generally be initiated as soon as possible when there is known influenza activity in the community. A history of current season influenza vaccination does not exclude a diagnosis of influenza in an ill child or adult. During influenza season especially, high-risk patients should be advised to call their provider promptly if they have symptoms of influenza. It may be useful for providers to implement phone triage lines to enable high-risk patients to discuss symptoms over the phone. To facilitate early initiation of treatment, when feasible, an antiviral prescription can be provided without testing and before an office visit.

Antiviral Medications

Three prescription neuraminidase inhibitor antiviral medications are approved by the U.S. Food and Drug
Administration (FDA) and are recommended for use in the U.S. during the 2017–2018 influenza season: oseltamivir (available as a generic version or under the trade name Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®).

- Oral oseltamivir is FDA-approved for treatment of uncomplicated influenza within 2 days of illness onset in persons aged 2 weeks and older, and for chemoprophylaxis to prevent influenza in people 1 year of age and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants younger than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year of age, is recommended by CDC and the American Academy of Pediatrics. Due to limited data, use of oseltamivir for chemoprophylaxis is not recommended in children younger than 3 months unless the situation is judged critical. CDC recommends oseltamivir treatment as

soon as possible for hospitalized patients with suspected or confirmed influenza, high-risk outpatients with suspected or confirmed influenza, and those with progressive disease.

- Inhaled zanamivir is FDA-approved for treatment of uncomplicated influenza within 2 days of illness onset in persons 7 years and older and for prevention of influenza in persons 5 years and older. Inhaled zanamivir is not recommended for treatment of influenza in hospitalized patients due to limited data.
- Intravenous peramivir is FDA-approved for the treatment of acute uncomplicated influenza within 2 days of illness onset in persons aged 2 years and older.

Adamantanes (rimantadine and amantadine) are not currently recommended for antiviral treatment or chemoprophylaxis of influenza A because of high levels of resistance among circulating influenza A viruses.

There are no current national shortages of neuraminidase inhibitors (i.e., oseltamivir, zanamivir and peramivir), and manufacturers report they expect to meet projected seasonal demands. If there is difficulty locating oseltamivir for oral suspension, as there has been in some previous seasons, oral suspension can be compounded by a pharmacy from oseltamivir capsules. However, this compounded suspension should not be used for convenience or when oseltamivir oral suspension is commercially available.

More information about compounding an oral suspension from oseltamivir 75 mg capsules can be found at https://www.gene.com/download/pdf/tamiflu_prescribing.pdf

Additional Considerations for Clinicians

- **Bacterial Infections:** Antibiotics are not effective against influenza virus infection, and early diagnosis of influenza can reduce the inappropriate use of antibiotics if bacterial co-infection is not suspected. However, because certain bacterial infections can produce symptoms similar to influenza and bacterial infections can occur as a complication of influenza, bacterial infections should be considered and appropriately treated, if suspected. In addition, because pneumococcal infections are a serious complication of influenza infection, current pneumococcal vaccine recommendations for adults 65 years of age or older, as well as adults and children at increased risk for invasive pneumococcal disease due to chronic underlying medical conditions, should be followed (see http://www.cdc.gov/vaccines/vpd-vac/pneumo/vac-PCV13-adults.htm and http://www.cdc.gov/vaccines/vpd-vac/pneumo/vacc-in-short.htm for further information).
- **Adverse Events and Antiviral Use**: The most common adverse events associated with oral oseltamivir include a slightly increased risk of nausea and vomiting as compared to placebo, with nausea occurring in 10% of adults with influenza who received oseltamivir and 6% of people who received placebo in controlled clinical trials (3% and 4%,

respectively, in children), and vomiting occurring in 9% of adults with influenza who received oseltamivir and 3% of people who received placebo in controlled clinical trials (15% and 9%, respectively, in children). These symptoms are generally transient and can be mitigated if oseltamivir is taken with food. Adverse events for inhaled zanamivir were not increased as compared to placebo in clinical trials, but cases of bronchospasm have been reported during post marketing; inhaled zanamivir is not recommended for persons with underlying airways disease (e.g., asthma or chronic obstructive pulmonary diseases). For people who received peramivir intravenously or intramuscularly in clinical trials, the most common adverse event was diarrhea, occurring in 8% versus 7% in people who received placebo.

Resources for Patient Education

Results from unpublished CDC qualitative research shows that most people interviewed were not aware that drugs to treat influenza illness are available. A fact sheet for patients is available at http://www.cdc.gov/flu/antivirals/whatyoushould.htm.

Additional Resources

- Summary of Influenza Antiviral Treatment Recommendations for Clinicians: http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm
- Clinical Description and Lab Diagnosis of Influenza: http://www.cdc.gov/flu/professionals/diagnosis/index.htm
- Guidance for Clinicians on the Use of RT-PCR and Other Molecular Assays for Diagnosis of Influenza Virus Infection: http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm
- Interim Guidance for Influenza Outbreak Management in Long-Term Care Facilities: http://www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm
  Influenza Virus Testing in Investigational Outbreaks in Institutional or Other Closed Settings: https://www.cdc.gov/flu/professionals/diagnosis/guide-virus-diagnostic-tests.htm
- FDA Influenza (Flu) Antiviral Drugs and Related Information (including package inserts): http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm100228.htm

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The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

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Alerting Message Specification Settings

Originating Agency:	Mississippi State Department of Health
Alerting Program:	MS Health Alert Network (MS HAN)
Message Identifier:	MSHAN-20171228-00409-ADV
Program (HAN) Type:	Health Advisory
Status (Type):	Actual ()
Message Type:	Alert
Reference:	MSHAN-00409
Severity:	Unknown
Acknowledgement:	No
Sensitive:	Not Sensitive
Message Expiration:	Undetermined
Urgency:	Undetermined
Delivery Time:	600 minutes

Definition of Alerting Vocabulary and Message Specification Settings

Originating Agency: A unique identifier for the agency originating the alert.

Alerting Program: The program sending the alert or engaging in alerts and communications using PHIN Communication and Alerting (PCA) as a vehicle for their delivery.

Message Identifier: A unique alert identifier that is generated upon alert activation (MSHAN-yyymmdd-hhmm-TTT (**ALT=Health Alert, ADV=Health Advisory, UPD=Health Update, MSG/INFO=Message/Info Service**).

Program (HAN) Type: Categories of Health Alert Messages**.**

Health Alert: Conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: Provides important information for a specific incident or situation; may not require immediate action.

Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action.

Health Info Service: Provides Message / Notification of general public health information; unlikely to require immediate action.

Status (Type):

Actual:	Communication or alert refers to a live event
Exercise:	Designated recipients must respond to the communication or alert
Test:	Communication or alert is related to a technical, system test and should be disregarded

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Message Type:

Alert:	Indicates an original Alert
Update:	Indicates prior alert has been Updated and/or superseded
Cancel:	Indicates prior alert has been cancelled
Error:	Indicates prior alert has been retracted

Reference: For a communication or alert with a Message Type of "Update" or "Cancel", this attribute contains the unique Message Identifier of the original communication or alert being updated or cancelled. "n/a" = Not Applicable.

Severity:

Extreme:	Extraordinary threat to life or property
Severe:	Significant threat to life or property
Moderate:	Possible threat to life or property
Minor:	Minimal threat to life or property
Unknown:	Unknown threat to life or property

Acknowledgement: Indicates whether an acknowledgement on the part of the recipient is required to confirm that the alert was received, and the timeframe in which a response is required (Yes or No).

Sensitive:

Sensitive:	Indicates the alert contains sensitive content
Not Sensitive:	Indicates non-sensitive content

Message Expiration: Undetermined.

Urgency: Undetermined. Responsive action should be taken immediately.

Delivery Time: Indicates the timeframe for delivery of the alert (15, 60, 1440, 4320 minutes (.25, 1, 24, 72 hours)).