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TO: Healthcare Providers, Hospitals, Long Term Care Facilities, Diagnostic and Treatment Centers, Pharmacies, and Local Health Departments

FROM: New York State Department of Health (NYSDOH) Division of Epidemiology

HEALTH ADVISORY: UPDATE ON INFLUENZA PREVENTION, SURVEILLANCE, AND CONTROL

For healthcare facilities, please distribute immediately to the Infection Control Department, Emergency Department, Infectious Disease Department, Director of Nursing, Medical Director, Director of Pharmacy, Primary Care Providers, and all patient care areas.

Summary
This advisory contains updated information about influenza activity in New York with links and references to important influenza resources.

Influenza Surveillance Summary

- Influenza activity abruptly began increasing during December 2014 and remains elevated.[1] Predominantly, influenza A (H3N2) viruses are causing disease during this influenza season[2]; however, influenza B and influenza A (H1N1)pdm09 have also been detected. It cannot be predicted with certainty which virus(es) will predominate for the remainder of the season.
- Historically, seasons dominated by A (H3N2) viruses have been more severe, resulting in large numbers of cases and hospitalizations. Additionally, A (H3N2) viruses disproportionately affect adults aged ≥65 years, young children, and persons with certain chronic medical conditions[3], and may lead to more severe outcomes. To date this season, adults aged ≥65 years have accounted for 61% of hospitalizations, but 30% of laboratory-confirmed cases.
- Similar to the national situation, most of the influenza A (H3N2) viruses that have been detected by the Wadsworth Center and characterized by CDC were antigenically "drifted" from the A/Texas/50/2012(H3N2) strain used for 2014-2015 vaccine production. Nationally, 35.7% of influenza A (H3N2) viruses, 100% of influenza A (H1N1)pdm09 viruses, 100% of influenza B Yamagata lineage, and 88.2% of influenza B Victoria lineage[4] viruses have been good antigenic matches to the stains used in the 2014-2015 vaccine.

Influenza Vaccine Recommendations

- The CDC early season influenza vaccine effectiveness study has shown that this season's influenza vaccine reduces a vaccinated person's risk of having to go to the doctor for flu

[1] https://www.health.ny.gov/diseases/communicable/influenza/surveillance/2014-2015/flu_report_current_week.pdf
[2] 98% of viruses identified by the Wadsworth Center have been A (H3N2) viruses.
[3] http://www.cdc.gov/flu/about/disease/high_risk.htm
[4] An influenza B Victoria lineage virus is currently included as a component of only quadrivalent vaccine formulations

illness by about 23% across all age groups. While offering reduced protection compared with some other seasons, this season's vaccine can still prevent infections with currently circulating strains and also lessen related complications.
- The NYSDOH continues to recommend that providers offer vaccine to all persons aged 6 months and older who have not yet been vaccinated. Vaccination is especially important for pregnant women, persons at high risk of complications, people who take care of, or live with, individuals who are at high risk, and all healthcare workers. Influenza vaccine remains available for purchase in NYS.

Antiviral Resistance and Supplies

- Nationally, no appreciable resistance to oseltamivir, zanamivir, or peramivir has been detected (0.1%; 1 oseltamivir and peramivir-resistant A (H1N1)pdm09 virus has been detected).
- Neither the FDA nor manufacturers of oseltamivir and zanamivir have identified a shortage. Genentech, the manufacturer of Tamiflu (oseltamivir), expects supply to be adequate for the 2014-2015 season.[5] However, local or regional spot shortages might occur when demand temporarily exceeds supply in those areas.
- Hospitals and pharmacies are encouraged to work through multiple distributors or suppliers to obtain antiviral medications.

Diagnostic Testing, Antiviral Treatment, and Chemoprophylaxis Recommendations

- Influenza antiviral treatment decisions should not be delayed pending testing results, nor should they be made based solely upon the results, particularly when rapid influenza diagnostic tests (RIDTs) are used. Detailed information regarding use and interpretation of influenza diagnostic tests is available at http://www.cdc.gov/flu/professionals/diagnosis/index.htm.
- CDC recommends antiviral medications for treatment and chemoprophylaxis of influenza. Current recommendations are at http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm, http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6001a1.htm, and http://emergency.cdc.gov/han/han00375.asp.
- Antiviral treatment is recommended as early as possible (ideally, within 48 hours of onset) for any patient with suspected or confirmed influenza who is hospitalized, has progressive, severe or complicated illness, or is at higher risk for influenza complications. Antiviral treatment also can be considered for any previously healthy, symptomatic outpatient not at high risk with confirmed or suspected influenza on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
- Antiviral chemoprophylaxis should be considered in community and institutional settings. The following are examples of situations where antiviral medications can be considered for chemoprophylaxis to prevent influenza:
    - Prevention of influenza in persons at high risk of influenza complications during the first two weeks following vaccination after exposure to an infectious person.
    - Prevention for people with severe immune deficiencies or others who might not respond to influenza vaccination, such as persons receiving immunosuppressive medications, after exposure to an infectious person.
    - Prevention for people at high risk for complications from influenza who cannot receive influenza vaccine due to a contraindication, after exposure to an infectious person.
    - Prevention of influenza among residents of institutions, such as long-term care facilities, during institutional outbreaks (http://www.cdc.gov/flu/professionals/infectioncontrol/ltc-

[5] http://www.gene.com/media/statements/ps_121814

facility-guidance.htm, http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Infuenza.pdf).

- Clinicians should remind patients that most persons with influenza have mild illness and do not need medical care. In most cases, persons with influenza should stay home and avoid contact with other people except to get medical care (http://www.cdc.gov/flu/homecare/). However, symptomatic persons who are at high risk of influenza complications, or who are severely ill or worried should be seen as soon as possible and antiviral treatment should be considered.

Influenza Prevention in Healthcare Settings

- Healthcare facilities should re-assess their adherence to recommendations about influenza prevention and control in healthcare settings (e.g., vaccination, minimizing potential exposures, and use of appropriate infection control practices, antiviral treatment, and chemoprophylaxis) which are available at http://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm.
- Guidance for influenza outbreak management in long-term care facilities is at http://www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm.
- Article 28 healthcare facilities should follow the recommendations for follow-up of respiratory disease outbreaks of influenza and influenza-like illness in health care facilities at http://www.health.ny.gov/diseases/communicable/control/respiratory_disease_checklist.htm.

Additional Information

Questions or concerns about surveillance, diagnostic testing, treatment, or chemoprophylaxis should be directed to the Bureau of Communicable Disease Control at 518-473-4439 (bcdc@health.ny.gov), except for those related to Article 28 healthcare facilities, which should be directed to the Bureau of Healthcare Associated Infections (BHAI) at 518-474-1142 (icp@health.ny.gov). Detailed information regarding ACIP 2014-2015 influenza vaccine recommendations is available at http://www.cdc.gov/flu/professionals/acip/index.htm. For additional information about vaccine, please contact the Bureau of Immunization at 518-473-4437 (immunize@health.ny.gov).

The CDC Health Advisory Regarding the Potential for Circulation of Drifted Influenza A (H3N2) Viruses: http://emergency.cdc.gov/HAN/han00359.asp.

The CDC Health Update Regarding Treatment of Patients with Influenza with Antiviral Medications: http://emergency.cdc.gov/han/han00375.asp.

CDC's Early Estimates of Seasonal Influenza Vaccine Effectiveness — United States, January 2015: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6401a4.htm?s_cid=mm6401a4_e.

Weekly updates of influenza surveillance in NYS: https://www.health.ny.gov/diseases/communicable/influenza/surveillance/.

Weekly nationwide influenza updates: http://www.cdc.gov/flu/weekly/fluactivitysurv.htm.

This is an official

CDC HEALTH UPDATE

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CDC Health Update Regarding Treatment of Patients with Influenza with Antiviral Medications

As a follow-up to HAN 00374 (http://emergency.cdc.gov/han/han00374.asp, Dec. 3, 2014), CDC is providing 1) a summary of influenza antiviral drug treatment recommendations, 2) an update about approved treatment drugs and supply this season, and 3) background information for patients regarding anti-influenza treatment.

Summary

Widespread influenza activity is being reported in most U.S. states, with influenza A (H3N2) viruses most common. H3N2-predominant flu seasons have been associated with more hospitalizations and deaths in older people and young children in the past. In addition, approximately two-thirds of H3N2 viruses that have been tested at CDC are antigenically or genetically different from the H3N2 vaccine virus. This difference suggests that vaccine effectiveness may be reduced this season. High hospitalization rates are being observed, similar to what was seen during the 2012-2013 influenza season. Hospitalization rates are especially high among people 65 years and older. In this context, the use of influenza antiviral drugs as an adjunct to vaccination becomes even more important than usual in protecting people from influenza. Antiviral medications are effective in treating influenza and reducing complications. Antivirals are available and recommended, but evidence from the current and previous influenza seasons suggests that they are severely underutilized.

This CDC Health Update is being issued

1) **to remind clinicians that influenza should be high on their list of possible diagnoses for ill patients, because influenza activity is elevated nationwide, and**
2) **to 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 one of three available influenza antiviral medications. This should be done *without* waiting for confirmatory influenza testing. While antiviral drugs work best when given early, therapeutic benefit has been observed even when treatment is initiated later.**

CDC Antiviral Recommendations for the 2014-2015 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, as evidenced from randomized controlled trials, meta-analyses of randomized controlled trials, and observational studies of oral oseltamivir, inhaled zanamivir, or parenteral peramivir treatment during past influenza seasons and during the 2009 H1N1 pandemic.

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

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

1) Is hospitalized – treatment is recommended for all hospitalized patients

2) Has severe, complicated, or progressive illness – this may include outpatients with severe or prolonged progressive symptoms or who develop complications such as pneumonia

3) Is at higher risk for influenza complications (hospitalized or outpatient) – 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);
- persons with immunosuppression, including that caused by medications or by HIV infection;
- women who are pregnant or postpartum (within 2 weeks after delivery);
- persons aged younger than 19 years who are receiving long-term aspirin therapy;
- American Indians/Alaska Natives;
- persons who are morbidly obese (i.e., body-mass index is equal to or greater than 40); and
- 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 early in the illness course. When indicated, 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.** Observational studies of hospitalized patients suggest that while the greatest benefit occurs when antiviral treatment is initiated within 48 hours of illness onset, treatment might still be beneficial when initiated up to 4 or 5 days after symptom onset. Also, a randomized placebo controlled study suggested clinical benefit when oseltamivir was initiated 72 hours after illness onset among febrile children with uncomplicated influenza. 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.

Because of the importance of early treatment, **decisions about starting antiviral treatment should not wait for laboratory confirmation of influenza**. Therefore, treatment should generally be initiated empirically. During influenza season especially, health care providers should advise high risk patients 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.

The results of rapid influenza diagnostic tests (RIDTs; immunoassays that can identify the presence of influenza A and B viral nucleoprotein antigens in respiratory specimens) may not be accurate; test sensitivities are approximately 50-70% when compared with viral culture or reverse transcription-polymerase chain reaction (RT-PCR). **Clinicians should realize that a negative RIDT result does not exclude a diagnosis of influenza in a patient with suspected influenza.** Other factors such as the quality of the specimen and timing of specimen collection may also affect test results. Rapid molecular assays are a new type of molecular influenza diagnostic test (http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm). Molecular testing is not needed for all patients with suspected influenza, but is most appropriate for hospitalized patients if a test result would lead to a change in clinical management.

Antivirals in Non-High Risk Patients with Uncomplicated Influenza

Neuraminidase inhibitors can benefit other individuals with influenza. While current guidance focuses treatment on those with severe illness or at high risk of complications from influenza, antiviral treatment may be prescribed on the basis of clinical judgment for any previously healthy (non-high risk) outpatient with suspected or confirmed influenza. Neuraminidase inhibitors reduce the duration of symptoms by ~1 day in healthy persons with uncomplicated influenza.

For previously healthy, symptomatic outpatients, if treatment is given, it is recommended that treatment be initiated within 48 hours of illness onset, although it is possible that treatment started after 48 hours may offer some benefit.

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 United States during the 2014-2015 influenza season: oseltamivir (Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®).

- Oral oseltamivir is FDA-approved for treatment of influenza 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 the 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.

- Inhaled zanamivir is FDA-approved for treatment of persons 7 years and older and for prevention of influenza in persons 5 years and older.

- Intravenous peramivir was approved on December 19, 2014, for the treatment of acute uncomplicated influenza in persons 18 years and older. An FDA press release related to this announcement is available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427755.htm.

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

There are no current national shortages of neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir). However, local spot shortages have been reported for some formulations. Therefore, it may be necessary to contact more than one pharmacy to fill a prescription for an antiviral medication.

If there is difficulty locating commercial Tamiflu® for Oral Suspension, oral suspension can be compounded by a pharmacy from oseltamivir capsules. However, this compounded suspension should not be used for convenience or when the FDA-approved Tamiflu® for Oral Suspension is commercially available.

Please see information for health care professionals regarding compounding an oral suspension from oseltamivir 75 mg capsules at http://www.tamiflu.com/hcp/resources/hcp_resources_pharmacists.jsp.

Additional Considerations for Clinicians

Antibiotics are not effective against influenza infection, and early diagnosis of influenza can reduce the inappropriate use of antibiotics. 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, new 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).

The most common adverse events associated with oral oseltamivir include a slightly increased risk of nausea and vomiting over 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 over placebo in clinical trials, but cases of bronchospasm have been reported during postmarketing; 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. Patients being provided a prescription for an influenza antiviral drug may have questions. A fact sheet for patients is available at http://www.cdc.gov/flu/antivirals/whatyoushould.htm.

Note the following important background information for patients:

- If you get the flu, antiviral drugs are a treatment option.
- It is very important that antiviral drugs are used early to treat hospitalized patients, people with severe flu illness, and people who are at high risk for flu complications because of their age, severity of illness, or underlying medical conditions.
- If you have severe illness or are at high risk of serious flu complications, you may be treated with flu antiviral drugs if you get the flu.
- For people with a high-risk condition, treatment with an antiviral drug can mean the difference between having milder illness instead of very serious illness that could result in a hospital stay.
- Other people also may be treated with antiviral drugs by their doctor this season. Most otherwise-healthy people who get the flu, however, do not need to be treated with antiviral drugs.
- Studies show that flu antiviral drugs work best for treatment when they are started within 2 days of getting sick. However, starting antivirals later can still be helpful for some people.
- If your health care provider thinks you have the flu, your health care provider may prescribe antiviral drugs. A test for flu is not necessary.
- Antibiotics are not effective against the flu. Using antibiotics inappropriately can lead to antibiotic resistance and may expose patients to unwanted side effects of the drug.
- Other practices that may help decrease the spread of influenza include respiratory hygiene, cough etiquette, social distancing (e.g., staying home from work and school when ill, staying away from people who are sick) and hand washing.

For More Information

- 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

- FDA Influenza (Flu) Antiviral Drugs and Related Information (including package inserts):
  http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm100228.htm