DELAWARE HEALTH ADVISORY #494: Interim Guidance to Prioritize Antiviral Treatment of Flu

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The Delaware Division of Public Health (DPH) is forwarding this advisory from the Centers for Disease Control and Prevention (CDC) providing interim guidance for clinicians to prioritize antiviral treatment of influenza in the setting of reduced availability of Oseltamivir.

Summary
Seasonal influenza activity is high across the United States. The CDC estimates that in the 2022-2023 season to date, there have been at least 13 million illnesses, 120,000 hospitalizations, and 7,300 deaths from influenza (Weekly U.S. Influenza Surveillance Report | CDC). While the Food and Drug Administration (FDA) has not indicated shortages of oseltamivir (generic or Tamiflu) in any of its forms (capsules, oral suspension), CDC has received numerous anecdotal reports of availability issues for generic oseltamivir in some locations [1]. This may continue to occur in some communities as influenza activity continues.

This Health Alert Network (HAN) Health Advisory provides clinicians and public health officials with guidance for prioritizing oseltamivir for treatment and information on other influenza antivirals that are recommended for treating influenza in areas where oseltamivir is temporarily unavailable.

Background
Antiviral treatment of influenza is an important adjunct to influenza vaccination in the prevention and control of influenza and, when given early, reduces the duration of symptoms and may reduce the risk of some complications [2-4].

Four FDA approved prescription antiviral medications (oseltamivir, baloxavir, zanamivir, and peramivir) are available for use for early treatment of outpatients with influenza. These antivirals have different formulations, routes of administration, dosing, duration of treatment, and recommendations for administration by age group. The clinical benefit of antiviral treatment of influenza is greatest when treatment is started early (within 2 days of illness onset) in people with mild, uncomplicated illness [3-4]. Oseltamivir treatment also is recommended as soon as possible for suspected or confirmed influenza requiring hospitalization, and to help control institutional influenza outbreaks [4].

Use of influenza testing, particularly rapid molecular assays, can inform antiviral treatment decisions, especially when other respiratory viruses are co-circulating in the community.

General Recommendations for Clinicians and Public Health Practitioners
Available information suggests that current local antiviral availability issues are due to limited availability of *generic* oseltamivir, specifically [1].

- If available, brand-name oseltamivir (Tamiflu) can be used to treat outpatients and hospitalized patients with influenza.
- If oseltamivir is unavailable, oral baloxavir, inhaled zanamivir, or intravenous peramivir can be used for early treatment of outpatients at increased risk for complications who present with uncomplicated influenza, depending upon age and contraindications.

- When there is limited availability of oseltamivir or other antivirals, antiviral treatment should target patients with influenza who are at the highest risk of severe disease and those who are hospitalized.
- Antiviral treatment of outpatients should be prioritized for persons who test positive for influenza within 2 days of illness onset.
- When there is limited availability of oseltamivir or other antivirals, patients with clinically mild influenza who are otherwise healthy and not at increased risk of influenza complications can be managed with supportive care without antiviral treatment.

Influenza Testing Considerations

- When antivirals are available, a clinical diagnosis of influenza without influenza testing can be made to support prescribing empiric antiviral treatment in outpatients.
- However, in settings where oseltamivir is currently unavailable, influenza testing for patients with suspected influenza is highly recommended to guide antiviral treatment.
- When there are limited supplies of antivirals, treatment of suspected influenza without a positive test result should be limited to those who are being hospitalized with suspected influenza, or patients highly suspected to have influenza (e.g., an ill patient who has a household member with laboratory-confirmed influenza).

Clinicians, hospitals, healthcare systems, and public health officials are encouraged to use all available information and their best judgment to prioritize oseltamivir and other antivirals for treating patients with influenza, depending upon their local situation. The following are considerations for antiviral treatment prioritization when antivirals such as oseltamivir are in short supply.

Guidance for Prioritization when Antiviral Supplies are Limited

Hospitalized Patients

- **Prioritize oseltamivir treatment as soon as possible for hospitalized patients with suspected or laboratory-confirmed influenza.**
    - Oseltamivir is the only antiviral that is recommended for treating influenza in hospitalized patients [4]. Because observational studies have shown that early initiation of oseltamivir treatment has significant clinical benefit [5-7], oseltamivir treatment is recommended to be started as soon as possible without waiting for results of influenza testing, such as in the emergency department or in admitted patients with high suspicion for influenza.
    - There are limited data for using inhaled zanamivir, intravenous peramivir, or baloxavir for treating influenza in hospitalized patients.
    - In a recent clinical trial, the addition of baloxavir to a neuraminidase inhibitor (primarily oseltamivir) did not show clinical benefit compared to neuraminidase inhibitor treatment alone in hospitalized patients with influenza aged 12 years and older [8].

Outpatients

Among outpatients, prioritize antiviral treatment for patients who test positive for influenza as follows:

- **Patients at increased risk of influenza complications and who test positive for influenza within two days of illness onset.**
    - People with multiple conditions that place them at increased risk for complications from influenza (e.g., several co-morbidities, age <2 years, and 65 years and older) and those

with severe uncontrolled chronic disease might be at highest risk of influenza complications.

- **Patients who have progressive or severe influenza not requiring hospitalization, even if they test positive for influenza more than two days from illness onset.**

- **Patients who are pregnant, less than two weeks postpartum, or immunocompromised**.
  - Substantial data from observational studies indicate that oseltamivir treatment of influenza is safe in pregnancy [9].
  - There are no data on the safety or efficacy of baloxavir in pregnancy and baloxavir is not recommended for pregnant people or those less than two weeks postpartum [9].
  - Treatment with a neuraminidase inhibitor (oseltamivir, zanamivir, or peramivir) is recommended for immunocompromised people with influenza.
  - Baloxavir is not recommended for treating influenza in immunocompromised people because the optimal duration of treatment is unknown and there is concern for emergence of influenza viruses resistant to baloxavir during or after treatment.

- **Children less than 5 years of age.**
  - Oseltamivir is the only recommended oral antiviral for treatment of influenza in children less than 5 years of age.
  - If oseltamivir suspension is unavailable for treating influenza in young children, clinicians can request that pharmacists compound a suspension from oseltamivir capsules.
  - In areas where generic oseltamivir is unavailable, baloxavir can be used for early treatment of influenza in otherwise healthy children aged 5 years and older, and for children aged 12 years and older with underlying conditions that increase their risk of influenza complications.

Institutional Settings

- **When an influenza outbreak is not occurring, prioritize oseltamivir for early treatment of influenza in residents of congregate settings such as long-term care facilities (LTCFs), who test positive for influenza.**

- **In the setting of laboratory confirmed influenza outbreaks in LTCFs:**
  - Early empiric antiviral treatment of suspected influenza in residents is recommended [4]. Once an influenza diagnosis is confirmed through testing, post-exposure antiviral chemoprophylaxis of exposed residents is recommended [4].
  - Because institutional outbreaks can be prolonged, consider using a limited duration treatment dosage (twice daily for five days) for post-exposure oseltamivir instead of extended use of oseltamivir chemoprophylaxis (once daily), with ongoing active daily monitoring and influenza testing for all residents with new illness signs and symptoms.
  - If oseltamivir is not available, baloxavir, zanamivir, or peramivir may be used for treatment of influenza.
  - Although baloxavir may be used for treatment, there are no available data on using baloxavir in LTCFs for treatment or post-exposure chemoprophylaxis.

Other Considerations

- In hospitalized patients, oseltamivir can be administered orally or enterically via oro- or nasogastric tube. For hospitalized patients who cannot absorb enterically-administered oseltamivir (e.g., due to gastric stasis, malabsorption, or gastrointestinal bleeding), or when oseltamivir is not available, intravenous peramivir is an option.
- For children who are not able to swallow prescribed oseltamivir capsules, the prescribed capsules may be opened and mixed with a thick sweetened liquid, such as chocolate syrup, prior to administration.
- When local generic oseltamivir availability issues are resolved, CDC recommends reverting back to original antiviral recommendations that include clinical diagnosis and empiric antiviral treatment of influenza in outpatients.
- Healthcare providers should use clinical judgement and all available data when making decisions about prescribing antibiotics to patients presenting with acute respiratory illness

Reporting

All cases of confirmed Influenza should be reported to the DPH Office of Infectious Disease Epidemiology (OIDE). Cases can be reported by phone (302-744-4990, normal business hours; 1-888-295-5156, outside of normal business hours), fax (302-622-4149), or email (reportdisease@delaware.gov).

For More Information

- CDC. Information for Clinicians on Influenza Virus Testing.
- CDC. Influenza Antiviral Medications: Summary for Clinicians.
- CDC. Interim Guidance for Influenza Outbreak Management in Long-Term Care and Post-Acute Care Facilities.
- CDC. Testing and Management Considerations for Nursing Home Residents with Acute Respiratory Illness Symptoms when SARS-CoV-2 and Influenza Viruses are Co-circulating.

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