LAC DPH Health Update

Antiviral Treatment and Chemoprophylaxis for Influenza Infection During SARS-CoV-2 Co-Circulation

November 10, 2022

This message is intended for all healthcare providers in Los Angeles County. Please distribute as appropriate.

Key Messages

- Healthcare providers must prepare for the possibility of a severe influenza season this fall and winter. All patients – especially those aged 65 years and older – should be urged at every healthcare encounter to get both their influenza vaccine and their updated fall COVID-19 booster as soon as possible.
- Influenza antiviral treatment should be initiated as soon as possible (within 48 hours of symptom onset) for patients with suspected or confirmed influenza who are: a) hospitalized; b) developing progressive disease; or c) at increased risk for influenza-associated complications. Do not wait for laboratory confirmation.
- CDC will be hosting a webinar *Seasonal Influenza Testing and Treatment During the COVID-19 Pandemic* on November 15 at 11 am PST. Free CME available. The recorded version will be available several hours after the live event. Webinar details.

Situation

CDC is reporting early increases of influenza activity throughout the country. This has been associated with an increase in influenza-related hospitalizations – with the highest hospitalization rates among older adults and young children. CDC has already reported the second pediatric influenza death of this new season. LA County surveillance data shows a similar increase in influenza activity with >10% of respiratory specimens testing positive for influenza, indicating that the 2022-2023 influenza season has begun.

Healthcare providers must be prepared for the possibility of a severe influenza season this fall and winter. Influenza antiviral treatments are an important adjunct to vaccination to prevent influenza-related morbidity and mortality. Although most people recover from uncomplicated influenza, influenza can cause complications that result in severe illness and death, particularly among very young children, older adults, pregnant persons, and people with certain chronic medical conditions.

In addition to influenza vaccination, influenza antivirals can shorten symptom duration and reduce the risk of influenza-related complications including pneumonia and respiratory failure. In hospitalized patients, early antiviral treatment of influenza has been shown to shorten inpatient stays in children and to reduce the risk of death in adults. The use of antiviral treatment in indicated patients with influenza might help alleviate stress on healthcare systems this season when multiple respiratory viruses are co-circulating.

Healthcare providers are encouraged to review the recent CDC Health Advisory about early, increased respiratory virus activity (influenza, respiratory syncytial virus [RSV], rhinovirus/enterovirus [RV/EV]) during continued SARS-CoV-2 circulation. CDC provides clinical guidance on the prevention and treatment of these co-circulating viruses, including when diagnostic testing is indicated.

Actions Requested of Providers

- **Continue to recommend and offer influenza vaccination for all eligible persons aged six months and older.** Note**:** persons 65 and older should be preferentially offered higher dose or adjuvanted vaccine (i.e., Fluzone High-Dose Quadrivalent vaccine, Flublok Quadrivalent recombinant flu vaccine and Fluad Quadrivalent adjuvanted flu vaccine).

  Vaccination is the best way to reduce the spread of influenza and reduce influenza illness and complications that can result in hospitalization and death. With this year's early start to the flu season, healthcare providers should urge all patients to get vaccinated as soon as possible. Both influenza and COVID-19 vaccines can be administered at the same visit, without regard to timing. If a patient is due for both vaccines, providers are encouraged to offer both vaccines at the same visit. Influenza vaccination efforts should continue throughout the flu season.

  See LAHAN on Fall Influenza and COVID-19 Vaccination

- **Start influenza antiviral treatment *as soon as possible* for adults and children with suspected or confirmed influenza who are:**

  - Hospitalized
  - Outpatients with severe, complex, or progressive disease (e.g., pneumonia, or exacerbation of underlying chronic medical conditions)
  - Outpatients at higher risk for complications; this includes children younger than 2 years of age, pregnant people, people who are up to 2 weeks post-partum (including following pregnancy loss), and adults aged 65 and older. See the CDC's complete list of people at higher risk.

  Antiviral therapy should be started ideally within 48 hours of symptom onset; do not wait for laboratory confirmation. Antiviral therapy may still provide some clinical benefits to hospitalized patients or those with severe, complicated, or progressive illness even when started more than 48 hours after illness onset.

  In addition, non-high-risk outpatients with suspected or confirmed influenza may be considered for antiviral treatment based on clinical judgement, if treatment can be initiated within 48 hours of symptom onset.

  The recommended antiviral treatment for hospitalized influenza patients, outpatients with severe, complex, or progressive illness, pregnant persons, and people who are up to 2 weeks post-partum is **oral oseltamivir.** For non-pregnant/post-partum outpatients with uncomplicated influenza who require antiviral treatment, alternative agents may be used depending on approved age groups and contraindications.

See Table below for a summary of recommended treatment regimens adapted from CDC Influenza Antiviral Medications: Summary for Clinicians.

For treatment recommendations for pregnant and postpartum people, see Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza

Considerations for patients co-infected with suspected or confirmed influenza and SARS-CoV-2

The NIH COVID-19 Treatment Guidelines recommend that hospitalized patients who are suspected of having either influenza or COVID-19 be started on empiric treatment for influenza with oseltamivir as soon as possible and without waiting for influenza test results.

Antiviral treatment for influenza is the same for all patients regardless of SARS-CoV-2 coinfection. There are no clinically significant drug-drug interactions between the antiviral agents or immunomodulators that are used to prevent or treat COVID-19 and the antiviral agents that are used to treat influenza.

- **Consider offering pre- and post-exposure chemoprophylaxis with influenza antivirals in selected situations.**

Although annual influenza vaccination is the best way to prevent influenza-associated infection and disease, providers should be aware of certain situations in which antiviral chemoprophylaxis can be considered as an adjunct to influenza prevention.

Pre-exposure chemoprophylaxis refers to providing antiviral medications to asymptomatic people in the absence of a known exposure to infectious influenza. CDC and IDSA do not recommend routine pre-exposure antiviral chemoprophylaxis. However, clinicians can consider pre-exposure prophylaxis in certain high-risk situations, such as persons at very high risk of complications from influenza or for whom the influenza vaccine is contraindicated or expected to have low effectiveness (e.g., severely immunocompromised). See IDSA guidelines for more situations when pre-exposure chemoprophylaxis might be useful and the recommended antiviral regimens for those indications.

Post-exposure chemoprophylaxis (PEP) refers to providing antiviral medications to asymptomatic persons who have an identifiable/potential exposure to infectious influenza. CDC does not recommend widespread or routine use of antiviral medications for post-exposure chemoprophylaxis. However, PEP is recommended as one of multiple interventions to control institutional influenza outbreaks (e.g., long-term care facilities, congregate residential settings, and hospitals). PEP may also be considered in rare circumstances for high-risk patients after exposure in non-institutional settings.

The following is a discussion of considerations for providing PEP. See Table below for appropriate chemoprophylaxis regimens. If symptoms develop, patients should be given antiviral therapy at treatment dosing.

- *Institutional outbreaks*
  - CDC recommends PEP with oral oseltamivir or inhaled zanamivir for a minimum of 2 weeks and continued for 7 days after the last known case was identified. PEP is recommended for all residents, including those who have received influenza vaccination.
  - **Note**: all outbreaks in institutional settings must be reported to Public Health immediately (see reporting below). Public Health will assist with managing the outbreak and will provide recommendations for PEP in these settings.
- *Non-institutional and community settings*
  - PEP can be considered for persons at high-risk for influenza complications (e.g., severely immunocompromised) if they have a known exposure to someone with influenza illness (such as a household contact of a confirmed influenza case). Antivirals should be provided within the first 48 hours after exposure.
  - In addition to oseltamivir and zanamivir, baloxavir can be used for PEP in non-institutional outpatient settings.
  - Baloxavir has a longer half-life (days) while the half-lives of oseltamivir and zanamivir are shorter (hours). Thus, for PEP, baloxavir can be administered as a single dose while oseltamivir and zanamivir require daily dosing for 7 days. ***Note****: baloxavir is not recommended for pregnant or breastfeeding individuals.*
  - **Note:** as an alternative to chemoprophylaxis, persons with known or suspected exposure to infectious influenza can be monitored closely with a plan for early initiation of antiviral treatment if fever and/or respiratory symptoms develop.
  - For further guidance on when to provide PEP see CDC and IDSA guidelines.

See table on next page

Antiviral Medications Recommended for the Treatment and Chemoprophylaxis of Influenza[1]

ORAL OSELTAMIVIR

Preferred *agent for hospitalized patients[2], pregnant individuals, and those up to 2 weeks post-partum[3]*

Adverse Effects: Nausea, vomiting, headache. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events

Treatment for any age

Duration of therapy: 5 days
Adults: 75 mg *twice* a day
Children 0-12 months: 3 mg/kg/dose *twice* a day
Children ≥12 months varies by weight:

- ≤15 kg: 30 mg *twice* a day
- >15 to 23 kg: 45 mg *twice* a day
- >23 to 40 kg: 60 mg *twice* a day
- >40 kg: 75 mg *twice* a day

Prophylaxis for ages 3 months and older

Duration of therapy: see note[4]
Adults: 75 mg *once* a day
Children 3-12 months: 3 mg/kg/dose *once* a day
Children ≥12 months varies by weight**:**

- ≤15 kg: 30 mg *once* a day
- >15 to 23 kg: 45 mg *once* a day
- >23 to 40 kg: 60 mg *once* a day
- >40 kg: 75 mg *once* a day

INHALED ZANAMIVIR

Not recommended for people with underlying respiratory disease (e.g., asthma, COPD).

Adverse Effects: Risk of bronchospasm, especially in the setting of underlying airways disease; sinusitis, and dizziness. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events.

Treatment for 7 years and older

Duration of therapy: 5 days
Adults and children ages ≥7 years: 10 mg (two 5-mg inhalations) *twice* a day

Prophylaxis for 5 years and older

Duration of therapy: see note[4]
Adults and children ages ≥5 years: 10 mg (two 5-mg inhalations) *once* a day

INTRAVENOUS PERAMIVIR

Adverse Effects: Diarrhea. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events

Treatment for 6 months of age and older

Duration of therapy: single infusion
Adults and Children ≥13 years: Single dose of 600 mg, via intravenous infusion for a minimum of 15 minutes
Children 6 months to 12 yrs of age: Single dose of 12 mg/kg, up to 600 mg maximum, via

intravenous infusion for a minimum of 15 minutes

Prophylaxis - not recommended

ORAL BALOXAVIR

Not recommended for pregnant or breastfeeding individuals.

Adverse Effects: None more common than placebo in clinical trials

Treatment and prophylaxis - for 5 years of age and older
Duration of therapy: Treatment - Single dose | Prophylaxis - Single dose for PEP in community settings
Adults varies by weight**:**

- <80kg: Single dose of 40 mg
- ≥80kg: Single dose of 80 mg

Children 5 yrs and older varies by weight**:**

- <20 kg: Single dose of 2 mg/kg by suspension
- 20 kg to <80 kg: Single dose of 40 mg by tablet or suspension
- ≥80 kg: Single dose of 80 mg by tablet or suspension

[1]Amantadine and rimantadine are not recommended antiviral treatments given high levels of resistance among circulating influenza A.

[2]Inhaled zanamivir and oral baloxavir are not recommended because of the lack of data showing clinical benefit in hospitalized influenza patients. There are also insufficient data for treatment of hospitalized influenza patients with intravenous peramivir.

[3]For further questions regarding treatment of high-risk populations please see CDC table footnotes.

[4]Duration of chemoprophylaxis is based on indication including pre-exposure prophylaxis or PEP in institutional vs non-institutional settings. Refer to IDSA guidelines for appropriate duration based on indication.

Table adapted from CDC Influenza Antiviral Medications: Summary for Clinicians Tables 1 and 2.

- **Report influenza cases as required**. The following influenza reporting is required:
    - **Any suspected outbreaks** in healthcare associated institutions, non-healthcare associated institutions, or congregate settings (*report immediately by phone*).
    - **All cases of suspected or confirmed "novel" influenza A infection**, including avian flu (H5N1 or H7N9) and swine flu (H3N2v, H1N1v, H1N2v) (*report immediately by phone*).
    - **Influenza-associated deaths** in laboratory confirmed cases, all ages. (*Report by electronic transmission – including fax or email – within 7 calendar days from identification*).

Refer to Reportable Diseases and Conditions for more reporting details

How to Report Influenza

Los Angeles County DPH Acute Communicable Disease Control:
Reporting immediately
- Weekdays 8:30am–5pm: call 213-240-7941.
- After-hours: call 213-974-1234 and ask for the physician on call.

Non-urgent reporting
- Fax a CMR to 888-397-3778 or 213-482-5508 or call 888-397-3993.

Long Beach Health and Human Services:
Reporting immediately
- Weekdays 8am-5pm: call 562-570-4302.
- After hours: call the Duty Officer at 562-500-5537.

Non-urgent reporting
- Fax the Long Beach CMR to 562-570-4374 or email LBEpi@longbeach.gov or call 562-570-4302.

Pasadena Public Health Department:
Reporting immediately
- Weekdays 8am-5pm: call 626-744-6089.
- After hours: call 626-744-6043.

Non-urgent reporting
- Fax a CMR to 626-744-6115 or email nursing@cityofpasadena.net or call 626-744-6089.

Additional Resources for Clinicians

- Summary of Influenza Antiviral Treatment Recommendations for Clinicians (CDC)
- Clinical Description and Lab Diagnosis of Influenza (CDC)
- Interim Guidance for Influenza Outbreak Management in Long-Term and Post-Acute Care Facilities (CDC)
- Influenza Virus Testing in Investigational Outbreaks in Institutional or Other Closed Settings (CDC)
- Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza A (IDSA)
- Influenza and COVID-19 (NIH COVID-19 Treatment Guidelines)

This communication was sent by Sharon Balter, MD, Director, Division of Communicable Disease Control and Prevention, Los Angeles County Department of Public Health

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