October 2020

CCHMC Community Practice Advisory Council

Influenza Update for Outpatient Providers

There is the potential this fall/winter for circulation of both Influenza and SARS-CoV-2. Influenza and SARS-CoV-2 infections have overlapping symptoms. It is possible for these infections to occur separately or as co-infections. A positive flu test does not preclude SARS-CoV-2, and a positive SARS-CoV-2 test does not preclude influenza. Testing can help distinguish. Flu testing during the season should be considered along with SARS-CoV-2 testing when it will impact care. Certain children are at higher risk for complications from either of these viruses. This document provides a brief review of IDSA and CDC guidance on influenza in children. Surveillance data on flu to help guide when to test for flu can be found on the CDC website here: https://www.cdc.gov/flu/weekly. **As always, flu vaccination for those over 6 months remains the most effective method of preventing flu.**

Who is considered HIGH RISK of influenza complications?

Children ≤2 years (<5 years increased risk but ≤ 2y at highest risk for treatment purposes (IDSA, AAP)

Adults ≥ 65 years

Women who are pregnant or postpartum during the season

Patients with immunosuppression attributable to any cause (including medication related)

Residents of chronic care facilities and nursing homes

America Indian and Alaskan native people

Patients with chronic disease including:

Neurologic or neurodevelopmental conditions (including intellectual disability, CP, MD, epilepsy, mod/severe DD)

Pulmonary disease (including COPD, CF, and asthma)

Blood disorders (including sickle cell disease)

Endocrine disorders

Heart disease (except hypertension alone)

Kidney disorders

Liver disorders

Metabolic disorders

Children and adolescents <19 yrs receiving long term ASA medication

Extreme obesity

Who needs testing for INFLUENZA in the outpatient (ED or clinic) setting during flu activity?

Lab testing is always recommended in patients requiring hospitalization for acute respiratory illness or worsening cardiopulmonary disease, with or without fever.

*Lab testing for flu might also be considered in the following outpatients IF THE RESULTS WILL INFLUENCE CLINICAL MANAGEMENT**:***

1. High risk patients
2. Patients with exacerbations of chronic illness (COPD, asthma, heart failure) or presenting with known complications of influenza (pneumonia)
3. Consider testing in non-high risk patients with influenza-like illness, pneumonia, or respiratory illness if results might influence antiviral treatment decisions or reduce use of unnecessary antibiotics, further diagnostic testing, time in ED, OR if results might influence antiviral treatment or chemoprophylaxis for high risk household contacts, including those who are pregnant

Note: Rapid influenza antigen tests are not be as sensitive as molecular tests.

When should antivirals be considered for influenza?

- Recommended for:
  - **All hospitalized patients** with confirmed, probable, or suspected influenza, **regardless of illness duration**
  - Outpatients of any age with severe or progressive illness, **regardless of illness duration**
  - Outpatients at **high risk** for seasonal influenza complications
  - Patients $\leq$ 2 years or $\geq$ 65 years
  - Clinicians can also consider treatment for:
    - Outpatients with symptom onset less than 2 days
    - Symptomatic outpatient household contact of high risk patients
    - Symptomatic healthcare providers caring for high risk patients
- Initiate therapy as soon as possible after onset of symptoms, preferably within 48 hours

Post- exposure chemoprophylaxis

- Consider for unvaccinated asymptomatic patients over 3 months who are at high risk of complications after household contact
- Consider for unvaccinated adults and children (in addition to vaccination) who are unvaccinated and household contacts of a person at very high risk of complications (severely immunocompromised) after exposure to influenza
- Alternative is **early empiric initiation of treatment**
- Post exposure prophylaxis **should not** be initiated over 48 hours after exposure

What are the treatment options?

Oral oseltamivir remains the antiviral of choice for the management of illness caused by influenza. Inhaled zanamivir is an acceptable alternative for patients who do not have chronic respiratory disease. Peramivir, a third NAI given IV, was approved in September 2017 as a treatment of acute uncomplicated influenza in non-hospitalized children who have been symptomatic for no more than 2 days. The FDA licensed baloxavir marboxil in 2018 for early treatment of uncomplicated influenza in patients 12 and older who have been ill no more than 2 days. It is prescribed as a single dose.

Treatment with oseltamivir for children with serious, complicated, or progressive disease presumptively or definitely caused by influenza, irrespective of influenza vaccination status, or whether illness began greater than 48 hours before admission, continues to be recommended by the AAP, CDC, IDSA and PIDS.

Dosing of Antivirals for Influenza (AAP/CDC/IDSA)

MEDICATION	TREATMENT (5 D)	CHEMOPROPHYLAXIS (7 D IDSA/CDC, 10 D AAP)	Possible adverse events
Oseltamivir (*Tamiflu*): 30, 45, 75 mg caps, 6mg/mL suspension			N/V, headache*, administration with meals may improve tolerability
Adult	75 mg BID	75 mg QD	
Children > 12 months			
Less than or = 15 kg (33 lbs.)	30 mg BID	30 mg QD	
151-23 kg (33-51 lbs.)	45 mg BID	45 mg QD	
231-40 kg (51-88 lbs.)	60 mg bid	60 mg QD	
Over 40 kg (88 lbs.+)	75 mg BID	75 mg QD	
Infants 9-11 months	*3.5 mg/kg/dose BID (AAP); 3.0 mg/kg/dose BID (CDC)*	*3.5 mg/kg/dose QD (AAP); 3.0 mg/kg/dose (CDC)*	
Term >40 wk infants 0-8 mo	3 mg/kg/dose BID	3-8 months old 3 mg/kg/dose QD; not recommended below 3 months	
Preterm infants	1.0 mg/kg/dose if less than 38 weeks postmenstrual age,	Not recommended	

	1.5 mg/kg/dose if 38-40 wk		
Peramivir (IV only) (*Rapivab*), single dose, limited data on influenza B, start within 48 h symptoms	>2-12 yr 12 mg/kg IV once, max 600 mg. Over 13 yr: 600 mg	Not recommended	Diarrhea
Inhaled Zanamivir (*Relenza*)			Bronchospasm if airway disease, sinusitis, dizziness, *
Adults	10 mg (two 5 mg inhalations) BID	10 mg (two 5 mg inhalations) QD	
Children (same dose)	≥7 y for treatment	≥5y for prophylaxis	
Baloxavir marboxil PO (*Xofluza*), 20 mg tabs			None
People ≥12 y &>40 kg	Not recommended for monotherapy in severely immunosuppressed patients; no available data on use more than 2 days after illness onset. Not recommended for treatment of pregnant or breastfeeding mothers.		
40-80 kg	One 40 mg dose, orally (2 20 mg tabs)	Not recommended	
At least 80 kg	One 80 mg dose, orally (2 40 mg tabs)	Not recommended	

Oseltamivir and Zanamivir had post-marketing reports of serious skin reactions and neuropsych events (self injury or delirium mainly reported in Japanese patients)

In a patient with suspected or confirmed influenza, when should bacterial co-infection of the upper or lower respiratory tract be considered, investigated, treated?

1. Patients who present with severe disease initially
2. Patients who deteriorate after initial improvement
3. Patients who fail to improve after 3-5 days of antiviral treatment

Streptococcus pneumoniae is the most common bacterial coinfection associated with influenza and pneumonia, but *S. aureus*, including MRSA, and *S. pyogenes* coinfections have also been reported in patients with pneumonia and influenza.

Sources for this document include IDSA (https://doi.org/10.1093/cid/ciy866), cdc.gov, and the 2020 AAP statement on influenza (pediatrics.aappublications.org/content/146/4/e2020024588)