MSHS Recommendations for Diagnosis and Treatment of Influenza 2019-2020

While seasonal influenza (flu) may be detected year-round, flu viruses are most commonly encountered during the fall and winter. The timing and duration of flu seasons varies; however, flu activity often begins to increase in October.
Encourage your colleagues, family, and patients to receive the influenza vaccine. Annual influenza vaccination is recommended for all persons ≥ 6 months of age in the absence of contraindications.[1]

Who to test for flu[2]:

1. In many cases the diagnosis of flu will be clinical. Testing is encouraged for high-risk patients (i.e., patients with underlying cardiac or pulmonary diseases and the immunocompromised).
2. Patients requiring admission for acute respiratory illnesses (ARI) including pneumonia, hospitalized patients with ARI without a clear alternative diagnosis, and in the ambulatory setting those where testing will affect clinical management should also be tested.
3. During flu season, acute exacerbations of chronic medical conditions like asthma, COPD, and heart failure may be due to flu and testing should be considered even if the patient does not present with a fever.

Treatment recommendations[2]:

1. If there is a suspicion of influenza, droplet precautions and therapeutic management should be initiated immediately. Do not delay the initiation of treatment pending test results. Ideally, treatment should be initiated within 48 hours of symptoms. However, treatment benefit has been demonstrated when initiated after 48 hours in some patients.
2. Most individuals without underlying medical conditions will have a self-limited respiratory illness. Those who present with an uncomplicated febrile illness generally do not require antiviral treatment. **They are encouraged to remain out of work or school until symptoms have resolved.**
3. When treatment is indicated, monotherapy with oseltamivir (Tamiflu®) or inhaled zanamivir (Relenza®) is sufficient. Antiviral resistance to these medications is rare. Dosing recommendations are below.
4. All hospitalized, severely ill, and high-risk patients with suspected or confirmed influenza should be treated with antivirals.

   Patients at high risk for influenza complications include:
   - Children ≤ 2 years old
   - Adults ≥ 65 years of age
   - Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss)
   - Persons ≤ 19 years who are receiving long-term aspirin therapy
   - American Indians/Alaska Natives
   - Morbidly Obese (BMI ≥ 40)
   - Residents of nursing homes and other chronic-care facilities
   - Persons with the following conditions:
     - Chronic pulmonary (including asthma), cardiovascular (except isolated hypertension), renal, hepatic, hematological (including sickle cell disease), 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, stroke, intellectual

disability, moderate to severe developmental delay, muscular dystrophy or spinal cord injury)
- Immunosuppression, including that caused by medications or by HIV or solid organ or stem cell transplantation

Antiviral dosing recommendations

Oseltamivir (Tamiflu®)		
ADULTS[3]		
Renal Function	**Treatment (5 days)**	**Chemoprophylaxis (7 days)**
Creatinine Clearance > 60	75 mg twice a day for 5 days	75 mg once daily for 7 days
Creatinine Clearance >30 – 60	30 mg twice a day for 5 days	30 mg once daily for 7 days
Creatinine Clearance 10 – 30	30 mg once a day for 5 days	30 mg every other day for 7 days
Creatinine Clearance <10*, NOT on hemodialysis	30 mg every other day for 5 days	Insufficient data for dosing recommendation*
Hemodialysis	30mg x1, then 30 mg after every hemodialysis cycle for 5 days	30mg x1, then 30 mg after alternate hemodialysis cycles for 7 days
Peritoneal Dialysis	30 mg x1 (1 dose total)	30 mg x1 (1 dose total) If needs > 7 days, then 30 mg once weekly immediately after dialysis exchange for the recommended duration of prophylaxis
CVVH[4]	75 mg twice daily for 5 days	75mg once daily for 7 days
CHILDREN† ≥ 12 months		
≤ 15 kg	30 mg twice a day for 5 days	30 mg once daily for 10 days
16-23 kg	45 mg twice a day for 5 days	45 mg once daily for 10 days
24-40 kg	60 mg twice a day for 5 days	60 mg once daily for 10 days
> 40 kg	75 mg twice a day for 5 days	75 mg once daily for 10 days
INFANTS[5] < 12 months		
9-11 months	3.5 mg/kg/dose twice a day for 5 days	3.5 mg/kg/dose once a day for 10 days
Term infants aged 0-8 months	3 mg/kg/dose twice a day for 5 days	≥ 3-8 months: 3 mg/kg/dose once a day for 10 days
		< 3 months: not recommended
Preterm infants	See footnote‡	

*Currently there are no treatment and/or prophylaxis data available for patients who are not on renal replacement therapy with a creatinine clearance ≤10. Please monitor for potential side effects.

† Renal dosing of oseltamivir is not published for pediatric patients.

‡ Current weight-based dosing recommendations are not appropriate for premature infants. Limited data from National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study group provides the basis for dosing preterm infants using postmenstrual age (gestational age + chronological age)[4]:

- < 38 weeks postmenstrual age: 1 mg/kg per dose orally twice daily
- 38 through 40 weeks post menstrual age: 1.5 mg/kg per dose orally twice daily
- > 40 weeks post menstrual age: 3 mg/kg per dose orally twice daily
- Extremely preterm infants (< 28 weeks), consult a pediatric infectious diseases physician

- Oseltamivir can be given via gastric tube; however gastric stasis or bleeding can reduce its absorption.
- Oseltamivir is available as 30 mg, 45 mg and 75 mg capsules and liquid for oral administration and is usually recommended to take with food to minimize nausea/vomiting.

Zanamivir (Relenza®)[3]		
ADULTS		
	Treatment (5 days)	**Chemoprophylaxis**
	10 mg (two 5 mg inhalations) twice a day	10 mg (two 5 mg inhalations) once a day for 7 days
CHILDREN[5]		
	≥ 7 years old for treatment	≥ 5 years old for prophylaxis
	10 mg (two 5 mg inhalations) twice a day	10 mg (two 5 mg inhalations) once a day for 10 days

- Please note that the oral inhalation formulation of zanamivir cannot be administered by nebulization. It is also not recommended for patients with underlying airway disease (asthma and COPD).
- Intravenous peramivir (Rapivab®) is non-formulary but is FDA-approved for the treatment of influenza in adult patients. Peramivir can be obtained if clinically indicated. Please discuss with Infectious Diseases or the Antibiotic Stewardship Program if peramivir is indicated.
- Baloxavir (Xofluza™) is non-formulary but is FDA-approved to treat influenza. It is approved for treatment of acute, uncomplicated influenza in the ambulatory setting and should not be used in pregnant women or children younger than 12 years of age pending further clinical data in these populations.

Chemoprophylaxis
Post-exposure chemoprophylaxis can be considered for individuals with following risks:

- Persons at higher risk for complications from influenza.
- Healthcare workers exposed to influenza (within 3 feet providing direct care or for a prolonged period) without adequate personal protective equipment (mask) or vaccination.

Chemoprophylaxis is generally not recommended if >48 hours have elapsed since last contact with the infectious person. Chemoprophylaxis for exposure to influenza is generally not recommended for persons who have received the influenza vaccine >14 days prior to exposure. In the setting of an outbreak or a high rate of vaccine breakthrough influenza, chemoprophylaxis may be offered irrespective of vaccination status. Chemoprophylaxis is not currently recommended for prevention of illness in healthy individuals.

Pregnant Women
Oseltamivir and zanamivir are "Pregnancy Category C" medications. Oseltamivir is preferred, but zanamivir may be considered due to its limited systemic absorption. Doses are the same as for non-pregnant adults.

Adverse Effects (AE)

Drugs	**Most Common Adverse Effects**
Oseltamivir	Nausea and/or vomiting (in up to 10%)
Zanamivir	Nasal signs and symptoms, cough, throat pain

Drug Interactions
Co-administration of oseltamivir with probenicid resulted in reduced clearance of oseltamivir by 50%. Co-administration of oseltamivir with warfarin can increase the risk of bleeding.

References:

1. Centers for Disease Control and Prevention. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices – United States, 2019-20 Influenza Season. *MMWR.* August 23, 2019: 68(3).
2. Uyeki TM *et al.* Clinical Practice Guidelines by the IDSA: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis.* 2019; 68(6): e1-47.
3. Influenza Antiviral Medications: Summary for Clinicians: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm accessed 6Sep2019
4. Eschenauer, G.A. & Lam, S.W. Intensive Care Med (2011) 37: 371.
5. AAP COMMITTEE ON INFECTIOUS DISEASES. Recommendations for Prevention and Control of Influenza in Children, 2018–2019. *Pediatrics.* 2018;142(4):e20182367