Influenza Treatment Protocol

I. Purpose

The purpose of this standing order is to reduce morbidity and mortality of influenza infection in Arkansas by allowing Arkansas-licensed pharmacists to initiate therapy including ordering and/or dispensing treatment medications, along with any necessary supplies for administration, to eligible persons who are influenza positive or who have household exposure.

II. Authority

This standing order is issued pursuant to Act 503 of 2021 (HB 1246) (Arkansas Code § 17-92-101) to authorize licensed pharmacists in Arkansas to order and/or dispense influenza treatment medications according to the provisions of Arkansas Code § 17-92-101 and the requirements of this standing order.

III. Screening and Assessment

The Board of Pharmacy will adopt screening assessment and questionnaire (Appendix A) to be used by pharmacists throughout the state. When a patient requests point-of-care testing services, or when a pharmacist, in his or her professional judgement, decides to initiate point-of-care testing and treatment, the patient will be assessed for presenting signs and symptoms that warrant influenza testing, parental consent for individuals under the age of 18, and if appropriate, administer a rapid influenza point-of-care test.

IV. Dispensing Guidelines

A. Eligibility Criteria

Inclusion:

- Age 3 years and older
- Reported symptoms or household exposure onset < 48 hours before time of presentation
- CLIA-waived point-of-care test for influenza virus is performed or household exposure

Exclusion:

- History of adverse reactions to any previous influenza treatment
- Pregnancy
- Use of antiviral therapy for influenza in the past **30 days**
- Flu-like symptoms for more than 48 hours
- Immunocompromised defined as:
    - Been receiving active cancer treatment for tumors or cancers of the blood

    - Received an organ transplant and are taking medicine to suppress the immune system
    - Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
    - Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
    - Advanced or untreated HIV infection
    - Active treatment with high-dose corticosteroids (20mg prednisone daily for >2 weeks) or other drugs that may suppress your immune response
- Clinically unstable based on the clinical judgement of the pharmacist or any of the following criteria:
    - Systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg
        - For age 3-9 years: Systolic blood pressure <70 + (age in years × 2)
    - Tachypnea (>25 breaths/min adult or >20 breaths/min <18 y/o)
    - Oxygen saturation (SpO_2) <90% via pulse oximetry

B. Contraindications

Do not administer oseltamivir to an individual with a known hypersensitivity to oseltamivir or any component of the formulation

Do not administer zanamivir to an individual with a known hypersensitivity to zanamivir or any component of the formulation (contains milk proteins)

Do not administer baloxavir to an individual with a known hypersensitivity (e.g., anaphylaxis, angioedema, urticaria, erythema multiforme) to baloxavir or any component of the formulation

C. Product Availability

Influenza treatment products that may be dispensed/provided under this standing order. Following dosing below, pharmacist can dispense any commercial available product form (tablet, capsule, suspension) based on availability and patient preference.

1. Oral Oseltamivir dosing:
    - **Adults, treatment:** 75 mg twice a day x 5 days
    - **Adults, prophylaxis:** 75 mg once daily x 7 days if vaccinated, 14 days if unvaccinated
    - **Children, treatment** Weight-based dosing x 5 days**:**
        - **15 kg or less:** 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

- **Children, prophylaxis**: Weight-based dosing x 7 days
  - **15 kg or less:** 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

2. Inhaled Zanamivir dosing:
   - **Adults, treatment**: 10mg (two 5mg inhalations) twice a day x 5 days
   - **Adults, prophylaxis**: 10mg (two 5mg inhalations) once daily x 7 days
   - **Children, treatment** (7 years or older): 10mg (two 5mg inhalations) twice a day x 5 days
   - **Children, prophylaxis** (5 years or older): 10mg (two 5mg inhalations) once daily x 7 days
   -
3. Oral Baloxavir dosing:
   - **Adults and Children 12 and older, treatment:**
     - **40 kg to less than 80kg:** single dose of 40 mg
     - **80 kg or more:** single dose of 80mg
   - **Adults, children 12 and older, prophylaxis**
     - **40 kg to less than 80kg:** single dose of 40 mg
     - **80 kg or more:** single dose of 80mg

D. Warnings/Precautions

1. Oseltamivir
   - Disease-related concerns
     - Cardiovascular disease: Use with caution in patients with chronic cardiac disease
     - Hepatic impairment: Use with caution in patients with severe hepatic impairment
     - Renal impairment: Use with caution; dosage adjustment is required for patients with renal impairment. Not recommended for patients with end stage renal disease (ESRD) not undergoing dialysis
     - Respiratory disease: Use with caution in patients with respiratory disease
   - Dosage forms specific issues
     - Some dosage form may contain sodium benzoate/benzoic acid which are metabolites of benzyl alcohol and have been associated with a potentially fatal toxicity in neonate ("gasping syndrome")
     - Oral suspension contains sorbitol (delivers ~2 g sorbitol per 75 mg dose) which is greater than the maximum daily limit for patients with hereditary fructose intolerance; may cause diarrhea and dyspepsia; use with caution
   - Appropriate Use

- Oseltamivir is not a substitute for the influenza virus vaccine. It has not been shown to prevent primary or concomitant bacterial infections that may occur with influenza virus. Antiviral treatment should begin within 48 hours of symptom onset; however, the CDC recommends that treatment may still be beneficial and should be started in patients with severe, complicated, or progressive illness, and in hospitalized patients if >48 hours. Treatment should not be delayed while awaiting results of laboratory tests for influenza. Outpatients who are not at high risk for developing severe or complicated illness are not likely to benefit if treatment is started >48 hours after symptom onset (CDC 2020a).

2. Zanamivir
   - Concerns related to adverse effects
     - Allergic reactions: Allergic-like reactions, including anaphylaxis, oropharyngeal edema, and serious skin rashes have been reported. Discontinue use and institute appropriate treatment if an allergic reaction occurs.
     - Neuropsychiatric events: rare occurrences of neuropsychiatric events (including confusion, delirium, hallucinations, seizure, and/or self-injury) have been reported, primarily in pediatric patients; may be abrupt in onset. Direct causation is difficult to establish; influenza infection may also be associated with behavioral and neurologic changes.
     - Respiratory effects: Bronchospasm, including serious cases and some with fatal outcomes, and decreased lung function have been reported in patients with and without airway disease; discontinue with bronchospasm or decreased lung function. For a patient with an underlying airway disease where a medical decision has been made to use zanamivir, a fast-acting bronchodilator should be made available.
   - Respiratory disease
     - Not recommended for use in patients with underlying respiratory disease, such as asthma or COPD, due to lack of efficacy in influenza treatment and risk of serious bronchospasm. If zanamivir is prescribed in such patients, closely monitor respiratory function.
   - Nursing home patients
     - Nursing home patients: Effectiveness has not been established for prophylaxis of influenza in nursing home patients (per manufacturer); however, the CDC recommends zanamivir as an option to be used to control institutional outbreaks of influenza (refer to current guidelines) (CDC 2020a).
3. Baloxavir
   - Bacterial infection
     - There is no evidence of efficacy of baloxavir marboxil in illnesses (eg, bacterial infections) caused by pathogens other than influenza viruses. Serious bacterial infections may begin with influenza-like symptoms, may

coexist with, or occur as an influenza complication. Baloxavir marboxil has not been shown to prevent such complications. Monitor for potential secondary bacterial infections and manage appropriately.

- Hypersensitivity
  - Hypersensitivity reactions, including anaphylaxis, angioedema, urticaria, and erythema multiforme have been reported; evaluate and treat accordingly.

E. Documentation

Positive influenza cases that result in hospitalization or death are required to be reported to the Arkansas Department of Health (ADH) at https://flureport.adh.arkansas.gov. To aid in influenza surveillance, ADH also encourages providers to report other positive influenza test results to the same website. Patient records must be furnished to a health care practitioner designated by the patient upon the request of the patient. Documentation may include, but is not limited to, presenting signs and symptoms that warrant influenza testing, parental consent for individuals under the age of 18, and results of RIDT. Maintain records of all patients receiving services for two (2) years.

APPENDIX A

Pharmacist Assessment, Evaluation and Prescribing Protocol Form: *Influenza*

PATIENT INFORMATION		
Name:	Date of Birth:	Age:
Address:	City/State/Zip:	
Email Address:	Phone:	
Primary Care Provider:		
Medication allergies?		
Current medications? (prescription, over-the-counter, herbals, topical medications, pain or allergy medication, and any supplements/vitamins)		
Treatments tried for the current condition (if none please indicate N/A):		

PATIENT ELIGIBILITY		
1. Are you 3 years of age and older?	❑ Yes	❑ No
2. Are you pregnant?	❑ Yes	❑ No
3. Have you ever been diagnosed with a weakened immune system? (e.g. cancer, transplant, or long term steroids)	❑ Yes* *Pharmacists see page 2, #4 for criteria	❑ No
4. When did your flu-like symptoms **start**?	❑ More than 2 days ago	❑ 2 days ago, yesterday or today
5. Do you have any of the following flu-like symptoms? (check all that apply)	❑ Fever ❑ Nasal congestion ❑ Muscle/body aches ❑ Cough ❑ Sore throat ❑ Other:_____	
6. Do you have any of the following? (check all that apply)	❑ History of allergic reactions to influenza treatment ❑ History of physiologic side effects from any previous influenza treatment ❑ Use of antiviral therapy for influenza in the **past 30 days** ❑ Received influenza (flu) vaccine within the past 12 months	

When complete, please return the form to pharmacy staff along with insurance information

-- FOR PHARMACY STAFF ONLY--

Physical Assessment	**REFER TO PCP** if determined clinically unstable or any of the following criteria
❑ Blood pressure:_____ ❑ RR:_____ ❑ %Oxygen:_____ ❑ Temperature:_____	❑ Systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg ❑ For age 3-9 years: Systolic blood pressure <70 + (age in years × 2) ❑ Tachypnea >25 breaths/min adult or >20 breaths/min <18 y/o ❑ Low oxygen <90% oxygen via pulse oximetry
CLIA-waived POCT Result	❑ Positive for influenza – continue ❑ Negative for influenza – refer to PCP + Symptomatic Treatment OR household post-exposure prophylaxis

Pharmacist Interpretation of qualifying questions and physical assessment; refer to PCP as appropriate. Exclusion criteria does not preclude from testing services. **Refer to PCP for treatment if:**

1. If patient is under 3 years of age **REFER TO PCP**
2. If patient is pregnant **REFER TO PCP**
3. If patient has had symptoms >48 hours **REFER TO PCP**
4. If patient is immunocompromised **REFER TO PCP**
    a. Been receiving active cancer treatment for tumors or cancers of the blood
    b. Received an organ transplant and are taking medicine to suppress the immune system
    c. Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
    d. Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
    e. Advanced or untreated HIV infection
    f. Active treatment with high-dose corticosteroids (20mg prednisone daily for >2 weeks) or other drugs that may suppress your immune response
5. If patient has history of adverse reactions to previous influenza treatment **REFER TO PCP**
6. If patient has used antiviral agents for influenza in the past 30 days **REFER TO PCP**

Treat using protocol if:

1. Age 3 years and older
2. Reported symptoms or household exposure onset < 48 hours before time of presentation
3. CLIA-waived point-of-care test for influenza virus is performed
    a. Symptomatic patient is positive for influenza virus via CLIA-waived point-of-care test
4. Household post-exposure prophylaxis

Diagnosis of Patient		
❑ Influenza ADULT ❑ Influenza Prophylaxis Adult	❑ Influenza CHILDREN and ADOLESCENTS ❑ Influenza Prophylaxis CHILDREN and ADOLESCENTS	❑ Refer to PCP

***the following can act as the prescription**

ADULT Therapy Options		
Influenza Adult **Treatment**		
❑ Oseltamivir	Dispense: ❑ 75mg #10 No refills	Sig: Take 1 (one) (75mg) by mouth twice daily for 5 days
❑ Zanamivir	Dispense: ❑ 1 inhaler No refills	2 inhalations by mouth twice daily for 5 days
❑ Baloxavir	Dispense: ❑ 40mg x 1 ❑ 80mg x 1 No refills	Take 1 tablet by mouth now
Influenza Adult **Prophylaxis**		
❑ Oseltamivir	Dispense: ❑ 75mg #7 ❑ 75mg #14 No refills	Sig: Take 1 (one) (75mg) by mouth once daily x 7 days Sig: Take 1 tablet by mouth once daily x 14 days
❑ Zanamivir	Dispense: ❑ 1 inhaler No refills	2 inhalations by mouth once daily x 7 days
❑ Baloxavir	Dispense: ❑ 40mg x 1 (if ≥40kg to 79kg) ❑ 80mg x 1 (if ≥ 80kg) No refills	Take 1 tablet by mouth now

Patient:_____.

Prescribed by:_____.

Signature:_____ Date:_____.

Follow-Up in 48 hours	
Assessment:	❑ If symptoms persist, refer to PCP

***the following can act as the prescription**

CHILDREN and ADOLESCENTS Therapy Options		
Influenza Children or Adolescent **Treatment** Weight (kg):_____		
❑ Oseltamivir	Dispense: Weight-based dosing ❑ ≤15kg: 30mg #10 ❑ 15-23kg: 45mg #10 ❑ 23-40kg: 60mg #10 ❑ >40kg: 75mg #10 No refills	Sigs: ❑ ≤15kg: 30mg by mouth BID x 5 days ❑ 15-23kg: 45 by mouth BID x 5 days ❑ 23-40kg: 60mg by mouth BID x 5 days ❑ >40kg: 75mg by mouth BID x 5 days
❑ Zanamivir	Dispense: ❑ 1 inhaler No refills	2 inhalations by mouth twice daily for 5 days
❑ Baloxavir	Dispense: ❑ 40mg x 1 ❑ 80mg x 1 No refills	Take 1 tablet by mouth now
Influenza Children or Adolescent **Prophylaxis** Weight (kg):_____		
❑ Oseltamivir	Dispense: Weight-based dosing ❑ ≤15kg: 30mg #7 ❑ 15-23kg: 45mg #7 ❑ 23-40kg: 60mg #7 ❑ >40kg: 75mg #7 No refills	Sigs: ❑ ≤15kg: 30mg by mouth daily x 7 days ❑ 15-23kg: 45 by mouth daily x 7 days ❑ 23-40kg: 60mg by mouth daily x 7 days ❑ >40kg: 75mg by mouth daily x 7 days
❑ Zanamivir	Dispense: ❑ 1 inhaler No refills	2 inhalations by mouth once daily x 7 days
❑ Baloxavir	Dispense: ❑ 40mg x 1 (if ≥40kg to 79kg) ❑ 80mg x 1 (if ≥ 80kg) No refills	Take 1 tablet by mouth now

Patient:_____.

Prescribed by:_____.

Signature:_____Date:_____.

Follow-Up in 48 hours	
Assessment:	❑ If symptoms persist, refer to PCP

References:

Infectious Diseases Society of America. Influenza Guidelines. http://www.idsociety.org

LexiComp. Wolters Kluwer Clinical Drug Information. http://online.lexi.com

Pediatric Vital Signs Reference Chart

Heart Rate (beats/min)		
Age	**Awake**	**Asleep**
Neonate (<28 d)	100-205	90-160
Infant (1-12 mos)	100-190	
Toddler (1-2 y)	98-140	80-120
Preschool (3-5 y)	80-120	65-100
School-age (6-11 y)	75-118	58-90
Adolescent (12-15 y)	60-100	50-90

Respiratory Rate (breaths/min)	
Age	**Normal**
Infant (<1 y)	30-53
Toddler (1-2 y)	22-37
Preschool (3-5 y)	20-28
School-age (6-11 y)	18-25
Adolescent (12-15 y)	12-20

Reference: PALS Guidelines, 2015

Blood Pressure (mmHg)				
Age		**Systolic**	**Diastolic**	**Systolic Hypotension**
Birth (12 h)	<1 kg	39-59	16-36	<40-50
	3 kg	60-76	31-45	<50
Neonate (96 h)		67-84	35-53	<60
Infant (1-12 mos)		72-104	37-56	<70
Toddler (1-2 y)		86-106	42-63	<70 + (age in years × 2)
Preschool (3-5 y)		89-112	46-72	
School-age (6-9 y)		97-115	57-76	
Preadolescent (10-11 y)		102-120	61-80	<90
Adolescent (12-15 y)		110-131	64-83	

Reference: PALS Guidelines, 2015
For diagnosis of hypertension, refer to the 2017 AAP guidelines Table 4 & 5:
http://pediatrics.aappublications.org/content/early/2017/08/21/peds.2017-1904

Temperature (°C)	
Method	**Normal**
Rectal	36.6-38.0
Tympanic	35.8-38.0
Oral	35.5-37.5
Axillary	36.5-37.5

Ranges do not vary with age.
Screening: axillary, temporal, tympanic (↓ accuracy)
Definitive: rectal & oral (↑ reflection of core temp.)
Reference: CPS Position Statement on Temperature Measurement in Pediatrics (2015)

Oxygen Saturation (SpO_2)

SpO_2 is lower in the immediate newborn period. Beyond this period, a SpO_2 of **<90-92%** may suggest a **respiratory condition** or **cyanotic heart disease**.

Dr. Chris Novak & Dr. Peter Gill for www.pedscases.com
(Edited March 2020 by Richard He)