Washington State Department of Health
Pharmacy Quality Assurance Commission
PO Box 47877
Olympia, WA 98504-7877

# Collaborative Drug Therapy Agreement for Antiviral Medications for Treatment or Prophylaxis during an Influenza Outbreak

I, _____, a licensed health care provider authorized to prescribe medication in the State of Washington, delegate prescriptive authority to _____ and the pharmacists listed below to initiate drug therapy for the treatment or prophylaxis of antiviral influenza according to the protocol that follows. The protocol provides written guidelines for the pharmacists to initiate drug therapy in accordance with the laws (RCW 18.64.011) and regulations (WAC 246-863-100) of the State of Washington.

- The protocol will be implemented only upon a written determination by the Local Health Officer that emergency procedures for dispensing antiviral medications are necessary in order to respond to an influenza outbreak.
- The pharmacists shall comply with the applicable local public health guidelines for outpatient antiviral drug use for influenza ("Local Public Health Guidelines"), which will be published during the influenza outbreak. The Local Public Health Guidelines will supersede when there is an inconsistency between the Guidelines and this protocol.
- The pharmacists shall document all drug therapy initiated under this protocol.
- As the authorizing prescriber, I or authorized staff under my supervision will be available to review the drug therapy initiated by the pharmacists.

This protocol will be in effect for two years unless rescinded earlier in writing to the Washington State Board of Pharmacy by either party. Any modification of the protocol shall be treated as a new protocol and filed with the Washington State Pharmacy Commission.

**Signatures of Responsible Parties:**

| _____ | _____ | _____ |
|---|---|---|
| Physician (MD or DO) or ARNP | License Number | Date |
| _____ | _____ | _____ |
| Pharmacist | License Number | Date |

**Pharmacists included in this protocol:**

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**Implementation of Protocol:**
This protocol will be implemented only upon a written determination by the Local Health Officer that emergency procedures for dispensing antiviral medications are necessary in order to respond to an influenza outbreak. The Local Health Officer will publish and distribute such a determination on the local public health web site and, if appropriate, through other communication channels in place during the response to the outbreak.

The Local Health Officer will be responsible for communication to the public regarding the availability of antiviral medications through this protocol.

When a patient presents to the pharmacy, the pharmacist will:

- Evaluate the patient in accordance with this protocol and applicable Local Public Health Guidelines and when deemed appropriate by the pharmacist, initiate drug therapy. Medications should be dispensed in the typical manner of processing a prescription order through the pharmacy's point of service system.
- Practice in accordance with the applicable Local Public Health Guidelines.
- Counsel the patient on the antiviral medication(s), symptom management, adverse side effect reporting, and self-referral to a primary provider or an emergency department upon development of severe symptoms or complications.
- Document the drug therapy initiated and subsequent side effects.
- Submit required documentation to the Local Health Officer for quality control evaluation after emergency antiviral dispensing has concluded.

**Patient Evaluation:**
The pharmacist must follow Local Public Health Guidelines for outpatient antiviral drug use. These guidelines will identify when antiviral treatment should be initiated for treatment based on the presence of flu signs and symptoms. The guidelines also will identify whether antiviral treatment should be initiated for prophylaxis and under what circumstances. Persons who are not at higher risk for complications or do not have severe influenza requiring hospitalization generally do not require antiviral medications for treatment or prophylaxis. Prophylaxis of certain close contacts of infected persons may be indicated during outbreaks, but general prophylaxis of the entire population with antiviral medication during epidemics is not. See Appendix 1 for the patient screening form.

Flu signs and symptoms include: fever, cough, sore throat, myalgias, arthralgias, headache, rhinorrhea, shortness of breath, chills and fatigue. Occasionally gastrointestinal symptoms may occur. When indicated and possible the pharmacist should take and record the patient's temperature.

Local Public Health Guidelines may contain specific recommendations for treatment or prophylaxis of patients and/or contacts at high risk of complications from influenza – so pharmacists should be aware of this patient population. Risk factors for severe disease with new pandemic strains of influenza are expected to overlap with may those for seasonal influenza but may not be identical. Patients should also be screened for factors that make them a high risk patient. These factors may include:

- Infants and children aged <5 years (Note: highest risk is for children under 2 years).
- Persons with asthma or other chronic pulmonary diseases, such as cystic fibrosis or chronic obstructive pulmonary disease
- Persons with chronic cardiac disease (such as congestive heart failure, coronary artery disease and structural heart disease but not hypertension)
- Persons who have immunosuppressive disorders or are receiving immunosuppressive therapy

- HIV-infected persons
- Pregnant women
- Persons with sickle cell anemia and other hemoglobinopathies
- Persons with diseases that require long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Persons with chronic renal dysfunction
- Persons with cancer
- Persons with chronic metabolic disease, such as diabetes mellitus
- Persons with neuromuscular disorders, seizure disorders, or cognitive dysfunction that may compromise the handling of respiratory secretions
- Adults aged >65 years
- Residents of any age of nursing homes or other long-term care institutions

Treatment should be initiated as early as possible because studies show that treatment initiated early (i.e., within 48 hours of illness onset) is more likely to provide benefit. However, some studies of hospitalized patients with seasonal influenza treated with oseltamivir have suggested benefit, including reductions in mortality or duration of hospitalization, even for patients whose treatment was started more than 48 hours after illness onset. Unless Local Public Health Guidelines state otherwise, patients who have been having symptoms for more than 48 hours AND are improving should not receive antivirals, but should be counseled on symptom management and to return to the pharmacy if their symptoms worsen into flu-like symptoms.

**Medications for Family Members:**
Unless Local Public Health Guidelines state otherwise, an individual may obtain prophylactic doses of antiviral medications for family members from the pharmacist. The individual acquiring antiviral medications needs to provide relevant medical history for the family member, and weight and age for children for dosing purposes. Drug therapy should not be initiated for persons whose medical information cannot be obtained. This situation is meant to allow parents and caregivers of children and high risk and medically frail patients to obtain medications for them.

**Referral:**
Patients may need to be referred to a physician or an emergency room. Drug therapy should be initiated before patients seek further care, if appropriate. Unless Local Public Health Guidelines state otherwise, patients should be evaluated for emergency warning signs (see below) and possibly referred if they have a fever that has lasted at least 24 hours and is exceeding:

- 100.5° F (38° C) in a patient less than 1 year old
- 101° F (38.3° C) in patients 1-17 years old
- 102° F (38.9° C) in adults

Pneumonia subsequent to an influenza infection is the leading cause of death from influenza. Patients with symptoms of pneumonia, including cough, fever, pleuritic chest pain, dyspnea, rigors, chills, and sputum production should be referred for urgent medical attention at a physician's office or an emergency department. Patients with other signs of life-threatening influenza complications, including cyanosis, central nervous system symptoms (sore neck and mental status changes) and extreme muscle pain need immediate emergency medical attention (eg. Call 911 or ED referral)

For **children**, emergency warning signs include:

- Fast breathing or trouble breathing
- Bluish or gray skin color (call 911 immediately)
- Not drinking enough fluids
- Severe or persistent vomiting
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough

For **adults**, emergency warning signs include:

- Difficulty breathing or shortness of breath
- Pain or pressure in the chest or abdomen
- Sudden dizziness
- Confusion
- Severe or persistent vomiting
- Flu-like symptoms improve but then return with fever and worse cough

**Procedures for Suspected Adverse Reactions:**
A patient who develops a suspected adverse reaction to an antiviral medication should call the pharmacy to report it. Pharmacists can recommend symptom management of the reaction, discontinuation of the medication, and/or patient referral. Development of life-threatening influenza symptoms should be immediately referred to the closest emergency room or urgent care clinic. Pharmacists should then report the adverse reaction to the FDA at MedWatch, found online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm or 1-800-FDA-1088. Patients can also report suspected adverse drug reactions directly to the FDA at MedWatch.

**Training:**
For pharmacists to participate in the protocol they must view the training slide set available online or as a handout and completely read this protocol and appendices. The protocol and slides can be found at www.wsparx.org.

**Documentation:**
Pharmacists must complete and retain the patient screening form for each patient. Documentation of antiviral medication(s) and doses initiated should also be included at the bottom of the form. Copies of the completed screening form should be submitted to the Local Public Health Office for evaluation of the protocol and to assess the number of doses distributed. Patient specific documentation should be made available to other healthcare providers if necessary for further treatment of the patient.

**Medications:**
Four prescription antiviral medications (oseltamivir (Tamiflu®), zanamivir (Relenza®), and the adamantanes, amantadine (Symmetrel) and rimantadine (Flumadine)are approved for treatment of influenza in the United States. Given the widespread resistance to amantadine and rimantadine among influenza A (H3N2) virus strains, oseltamivir and zanamivir have been the only recommended single use agents. Recent seasonal influenza A H1N1 strains have been resistant to oseltamivir while the new pandemic influenza A 2009 H1N1 virus remains largely sensitive oseltamivir at this time. Strains resistant to oseltamavir and zanaminivir may occur and treatment with two antiviral medications, an adamantane with oseltamavir or zanaminivir, may be recommended. Local Public Health Guidelines will

contain recommendations for the use of antiviral medication(s) in the setting of oseltamivir resistance among circulating influenza strains, if necessary.

The following dosing recommendations may be superseded by Local Public Health Guidelines during the outbreak. **The manufacturer's medication package inserts and Section 1 of the Prescribing Tool Kit contain detailed prescribing information including information on contraindications, precautions, pregnancy, nursing mothers and adverse reactions.**

**1) Oseltamivir phosphate** (**Tamiflu®)** capsules (30 mg, 45 mg, 75 mg) and oral suspension (12 mg/mL) (capsules may be used for emergency compounding of an oral suspension; directions available at http://www.rocheusa.com/products/tamiflu/pi.pdf) (Adapted from Oseltamivir [package insert], Roche 2008 and CDC recommendations)

**Indications and usage:**

-**Treatment** of uncomplicated acute illness due to influenza infection in patients 1 year and older who have been symptomatic for no more than 2 days

-**Prophylaxis** of influenza in patients 1 year and older

**Dosage and administration:**

| Adults & adolescents ≥13 years | Treatment for 5 days | Prophylaxis for 10 days |
|---|---|---|
| Normal Renal Function | 75 mg orally twice daily | 75 mg orally once daily |
| -CrCl 10-30mL/min | 75 mg orally once daily | 75 mg orally every other day OR 30 mg once daily |
| -Hemodialysis* | 30 mg orally twice weekly (during alternate HD sessions) for 2 doses total | 30 mg orally twice weekly (during alternate HD sessions) for 2 doses total |
| -peritoneal dialysis (CAPD)* | 30 mg orally once weekly for 1 dose total | 30 mg orally once weekly for 1 dose total |

* (Robson R, Buttimore A, Lynn K, et al. The pharmacokinetics and tolerability of oseltamivir suspension in patients on hemodialysis and continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 2006; 21:2556-62.

| Children ≥1 year with body weight (kg): | Treatment for 5 days | Prophylaxis for 10 days |
|---|---|---|
| ≤ 15 | 30 mg orally twice daily | 30 mg orally once daily |
| >15-23 | 45 mg orally twice daily | 45 mg orally once daily |
| >23-40 | 60 mg orally twice daily | 60 mg orally once daily |
| >40 | 75 mg orally twice daily | 75 mg orally once daily |

| Infants <1 year:** | Treatment for 5 days | Prophylaxis for 10 days |
|---|---|---|
| < 3 months | 12 mg orally twice daily | **Not recommended |
| 3-5 months | 20 mg orally twice daily | 20 mg orally once daily |
| 6-11 months | 25 mg orally twice daily | 25 mg orally once daily |

** Depends on whether a FDA emergency use authorization (EUA) has been issued to use antiviral medications in patients less than 1 year of age if appropriate for the situation.

**2) Zanamivir (Relenza®)** for inhalation (Adapted from Zanamivir [package insert], GSK 2008)

**Indications and usage:**
-Treatment of uncomplicated acute illness due to influenza A and B virus in adult and pediatric patients 7 years of age and older who have been symptomatic for no more than 2 days
-Prophylaxis of influenza in adult patients and pediatric patients 5 years of age and older

**Dosage and administration:**
-**Treatment in adults and pediatric patients 7 years and older**: 2 inhalations (one 5 mg blister per inhalation for a total dose of 10 mg) **twice** daily (approximately 12 hours apart) for 5 days
Two doses should be taken on the first day of treatment whenever possible provided there is at least 2 hours between doses
**Prophylaxis:**
**Household setting: in adults and pediatric patients 5 years of age and older:** 12 inhalations (10 mg) **once** daily for 10 days
(There is no data on the effectiveness of prophylaxis with Relenza in a household setting when initiated more than 1.5 days after the onset of signs and symptoms in the index case.)
**Dose adjustments**: none

**3) Rimantadine hydrochloride** (tablets 100 mg; Flumadine syrup 50 mg/5mL) (Adapted from Rimantadine [package insert], Sandoz 2007)

**Indications and usage:**
-Prophylaxis and treatment of illness caused by various strains of influenza A virus in adults
-Prophylaxis against influenza virus in children
(In controlled studies of children over the age of 1 year, healthy adults and elderly patients, rimantadine hydrochloride has been shown to be safe and effective in preventing signs and symptoms of infection caused by various strains of influenza A virus.)
Rimantadine has not been approved by the US FDA for treatment of children, but published data exist on safety and efficacy in the pediatric population (Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults in children- diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 2009; 48:1003-32.)

**Dosage and administration:**

| | Treatment for 7 days from initial onset of symptoms | Prophylaxis |
|---|---|---|
| Adults | 100 mg orally twice daily | 100 mg orally twice daily |
| Adults with severe hepatic dysfunction, renal failure (CrCl $\leq$10 mL/min) and elderly nursing home patients | 100 mg orally once daily | 100 mg orally once daily |
| Children age 1-9 years | 6.6 mg/kg per day, but not exceeding 150 mg (divided into 2 doses) | 5 mg/kg per day, but not exceeding 150 mg |
| Children age $\geq$10 years | 100 mg orally twice daily | 100 mg orally twice daily |

**4) Amantadine hydrochloride** (capsules, tablets 100 mg; syrup 50 mg/5mL)

**Indications and usage:**
Prophylaxis and treatment of signs and symptoms of infection caused by various strains of influenza A virus

**Dosage and administration:**
-**Prophylaxis and treatment in adults**: 200 mg once daily or 100 mg twice daily for 7 days from initial onset of symptoms (If central nervous system effects develop in once-a-day dosage, a split dosage schedule may reduce such complications.)
**Dose adjustments:**
In patients ≥65 years of age: 100mg once daily
In patients with impaired renal function

| CrCl (mL/min) | Dosage |
|---|---|
| 30 to 50 | 200 mg first day, then 100 mg each day after |
| 15 to 29 | 200 mg first day followed by 100 mg on alternate days |
| <15 or hemodialysis | 200 mg every 7 days |

-**Prophylaxis and treatment in children**:
Ages 1 to 9 years: 4.4-8.8 mg/kg per day; not to exceed 150 mg/day
Ages 9 to 12 years: 100 mg orally twice daily