State of California—Health and Human Services Agency
California Department of Public Health

SANDRA SHEWRY, MPH, MSW
Acting Director

GAVIN NEWSOM
Governor

CDPH Influenza Antiviral Guidance for Shelter Residents, October 2020

The public health recommendations in this document are based on existing guidance regarding the use of antiviral medications for treatment and chemoprophylaxis of influenza in the general population and in long-term care facilities.[1,2] The goals of this guidance are 1) to prevent morbidity due to influenza in shelter residents and 2) to prevent transmission of influenza among shelter residents, both by decreasing viral shedding by ill residents, and by protecting well contacts of influenza cases from influenza illness.

Influenza vaccination of shelter residents and staff and the prompt separation of those with influenza-like illness (ILI) from others remain the primary strategies for prevention of influenza in the shelter setting. Social distancing, masking, and other strategies to prevent COVID-19 transmission should also reduce transmission of influenza and other respiratory diseases. During influenza season, residents or staff members with ILI should be tested for both influenza and COVID-19; while test results are pending, the resident or staff member with ILI should be isolated according to guidance for managing suspected cases of COVID-19.
This document does not replace clinical decision-making with respect to individual care of residents. Residents who are clinically unstable should be transferred to a medical facility as soon as feasible.

Influenza-like illness (ILI)

- ILI is defined as fever (temperature of 100°F [37.8°C] or greater) and a cough and/or a sore throat in the absence of a KNOWN cause.
- Individuals who are frail, elderly, and/or with weakened immune systems may be less likely to mount a fever, and clinical decision-making should be used regarding residents who do not meet all criteria for ILI but might have influenza or another respiratory infection.

---

[1] CDC. Antiviral Drugs – Information for Health Care Professionals. https://www.cdc.gov/flu/professionals/antivirals/index.htm. Accessed 6 October 2020.

[2] California Department of Public Health. Recommendations for the Prevention and Control of Influenza in California Skilled Nursing Facilities (SNF). Updated October 2020. https://www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/SNF_DetectAndControlOutbreaks.aspx

Antiviral medications

Oseltamivir is the first-line oral agent recommended for influenza antiviral treatment and chemoprophylaxis. Note that treatment dosing differs from chemoprophylaxis dosing, and residents with impaired renal function require adjusted doses. Antiviral dosing tables are provided at the end of this document. Inhaled Zanamivir is an option for those who cannot receive oral oseltamivir, but zanamivir should not be used in people with underlying respiratory disease due to risk of bronchospasm. Baloxavir (oral) has been approved for treatment of influenza for individuals 12 years and older, and Peramivir (intravenous) has been approved for treatment of influenza for individuals 2 years and older, but these antivirals are not recommended for chemoprophylaxis.

Antiviral treatment for residents with influenza or ILI

- To decrease transmission of influenza, offer antiviral treatment promptly to shelter residents with laboratory-confirmed influenza or ILI, pending laboratory confirmation. Treatment is especially important for residents who are at high risk for complications of influenza, such as pregnant women and those who are immunocompromised, <2 years of age, or ≥65 years of age, and those with pre-existing medical conditions.
- While treatment started within 48 hours of symptom onset is most effective, treatment started later can still be beneficial, especially for individuals at higher risk for severe illness and/or complications.
- Do not decide against or discontinue antiviral treatment based on a negative rapid influenza diagnostic test (RIDT).
    - A negative RIDT result should be confirmed with PCR testing at a clinical or public health lab.
    - Because of the need for accurate diagnostic testing results in the shelter setting, polymerase chain reaction (PCR) testing is recommended. PCR testing is available at many clinical and public health laboratories. If possible, Influenza and SARS-CoV-2 testing should be conducted simultaneously on shelter residents with ILI.

Antiviral chemoprophylaxis for close contacts of residents with influenza

- In the shelter setting, close contacts are residents with beds within 6 feet of the ill resident's bed, and family members, friends or other shelter residents or staff with whom the resident has had extensive face-to-face contact (such as eating meals or socializing together) from one day before symptom onset until separation from others was initiated.
- Antiviral chemoprophylaxis should be offered to close contacts of residents with laboratory-confirmed influenza, whether or not they have received an influenza vaccine.
- Consideration should be given to offering antiviral chemoprophylaxis to contacts of residents with ILI who are at high risk of influenza complications due to age and/or

underlying medical conditions, while the ill resident's influenza test result is pending. (See treatment and chemoprophylaxis dosing tables at the end of this document).

- Unvaccinated close contacts of residents with influenza should be offered influenza vaccine, whether or not they receive antivirals.
- Antiviral chemoprophylaxis should ideally be started within 48 hours of the most recent exposure to the ill individual. It should be continued for 10 days after the most recent exposure to the ill individual. Antiviral chemoprophylaxis should not be discontinued based on the ill resident testing negative on a RIDT. A negative RIDT result should be confirmed with PCR testing at a clinical or public health lab.
- Individuals receiving chemoprophylaxis should be instructed to report any symptoms of ILI to shelter personnel. They should be informed that chemoprophylaxis lowers but does not eliminate the risk for influenza, and that susceptibility to influenza returns once the antiviral medication is stopped.
- Residents who develop influenza after taking antiviral chemoprophylaxis for 72 hours or more should be reported to the local health department so that the possibility of resistance to the antiviral agent used can be considered.

Antiviral chemoprophylaxis for healthcare personnel and other staff caring for shelter residents with influenza or ILI

- Unimmunized healthcare personnel or other staff who are providing care to shelter residents with influenza should be offered immunization and may be offered chemoprophylaxis.

Special circumstances

- Residents with laboratory-confirmed influenza should be isolated from others either until they have been afebrile for 24 hours without use of antipyretic medications or according to public health guidance, whether or not they are treated with antivirals. Residents with ILI or laboratory-confirmed influenza should not be cohorted with residents with laboratory-confirmed COVID-19.
- If influenza activity in a specific shelter is unusually widespread, and if the population of the shelter predominantly consists of individuals at high-risk for complications, consideration may be given to offering chemoprophylaxis to a wider group of shelter residents. This decision would be made on a case-by-case basis in consultation with state and local public health authorities.

Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza*

Antiviral Agent	Activity Against	Use	Recommended For	Not Recommended for Use in	Adverse Events
Oral Oseltamivir	Influenza A and B	Treatment	Any age[1]	N/A	**Adverse events:** nausea, vomiting, headache. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemoprophylaxis	3 months and older[1]	N/A	
Inhaled Zanamivir	Influenza A and B	Treatment	7 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	**Adverse events:** 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[2]
		Chemoprophylaxis	5 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	
Intravenous Peramivir	Influenza A and B[4]	Treatment	2 yrs and older[4]	N/A	**Adverse events:** diarrhea. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemoprophylaxis[5]	Not recommended	N/A	
Oral Baloxavir	Influenza A and B[6]	Treatment	12 yrs and older[6]	N/A	**Adverse events:** none more common than placebo in clinical trials
		Chemoprophylaxis[5]	Not recommended	N/A	

Abbreviations: N/A = not applicable, COPD = chronic obstructive pulmonary disease.

[1] Oral oseltamivir phosphate is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older, and for chemoprophylaxis in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics. If a child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless the situation is judged critical due to limited data in this age group.

[2] Self-injury or delirium; mainly reported among Japanese pediatric patients.

[3] Inhaled zanamivir is contraindicated in patients with underlying airways disease such as asthma or chronic obstructive pulmonary disease, and those with a history of allergy to lactose or milk protein.

[4] Intravenous peramivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 2 years and older. Peramivir efficacy is based on clinical trials versus placebo in which the predominant influenza virus type was influenza A; in one trial, a very limited number of subjects infected with influenza B virus were enrolled.

[5] There are no data for use of peramivir or baloxavir for chemoprophylaxis of influenza.

[6] Oral baloxavir marboxil is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 12 years and older who are otherwise healthy, or at high risk of developing influenza-related complications. The safety and efficacy of baloxavir for the treatment of influenza have been established in pediatric patients 12 years and older weighing at least 40 kg. Baloxavir efficacy for initial FDA approval in October 2018 was based on clinical trials in previously healthy outpatients 12 to 64 years old (Hayden, 2018). Single-dose baloxavir treatment was superior to placebo and had similar clinical efficacy in time to alleviation of symptoms to a 5-day treatment course of oseltamivir. In October 2019, FDA approved an indication for baloxavir treatment of acute uncomplicated influenza within 2 days of illness onset in people 12 years and older at high risk of developing influenza-related complications, based upon the findings of a clinical trial (Ison, 2020; Baloxavir marboxil [Xofluza] package insert). U.S. Food and Drug Administration website; 2019). In this clinical trial of early initiation of antiviral treatment for uncomplicated influenza in high-risk patients, baloxavir was superior to placebo and had similar overall efficacy to oseltamivir in the time to alleviation of symptoms. For patients with influenza B virus infection, baloxavir significantly reduced the median time to improvement of symptoms compared with oseltamivir by more than 24 hours. However, there are no available data for baloxavir treatment of influenza in pregnant women, immunocompromised people, or in people with severe influenza. There are no available data from clinical trials for baloxavir treatment of hospitalized patients with influenza.

Table 2. Recommended Dosage and Duration of Influenza Antiviral Medications for Treatment or Chemoprophylaxis*

Antiviral Agent	Use	Children	Adults
Oral Oseltamivir	Treatment (5 days)[1]	**If younger than 1 yr old**[2]: 3 mg/kg/dose twice daily[3,4] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **twice** a day > 15 to 23 kg, the dose is 45 mg **twice** a day > 23 to 40 kg, the dose is 60 mg **twice** a day > 40 kg, the dose is 75 mg **twice** a day	75 mg **twice** daily
	Chemo-prophylaxis (7 days)[5]	If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical due to limited data in this age group. **If child is 3 months or older and younger than 1 yr old**[2] 3 mg/kg/dose once daily[3] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **once** a day > 15 to 23 kg, the dose is 45 mg **once** a day > 23 to 40 kg, the dose is 60 mg **once** a day > 40 kg, the dose is 75 mg **once** a day	75 mg **once** daily
Inhaled Zanamivir[6]	Treatment (5 days)	10 mg (two 5-mg inhalations) **twice** daily (**FDA approved and recommended for use in children 7 yrs or older**)	10 mg (two 5-mg inhalations) **twice** daily
	Chemo-prophylaxis (7 days)[5]	10 mg (two 5-mg inhalations) **once** daily (**FDA approved for and recommended for use in children 5 yrs or older**)	10 mg (two 5-mg inhalations) **once** daily
Intravenous Peramivir[7]	Treatment (1 day)[1]	(2 to 12 yrs of age) One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for a minimum of 15 minutes (**FDA approved and recommended for use in children 2 yrs or older**)	(13 yrs and older) One 600 mg dose, via intravenous infusion for a minimum of 15 minutes
	Chemo-prophylaxis[8]	Not recommended	N/A
Oral Baloxavir[9]	Treatment (1 day)[1]	**FDA approved and recommended for use in children 12 yrs or older weighing at least 40 kg**. See adult dosage.	(12 yrs and older) 40 to 80 kg: One 40 mg dose; ≥80 kg: One 80 mg dose[9]
	Chemo-prophylaxis[8]	Not recommended	N/A

Abbreviations: N/A = not approved

[1] Longer treatment duration may be needed for severely ill patients.

[2] Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset with twice-daily dosing in people 14 days and older, and for chemoprophylaxis with once-daily dosing in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year of age, is recommended by the CDC and the American Academy of Pediatrics (Committee on Infectious Diseases, 2018).

[3] This is the FDA-approved oral oseltamivir treatment dose for infants 14 days and older and less than 1 year old, and provides oseltamivir exposure in children similar to that achieved by the approved dose of 75 mg orally twice daily for adults, as shown in two studies of oseltamivir pharmacokinetics in children (Kimberlin, 2013 [CASG 114], EU study WP22849, FDA Clinical Pharmacology Review). The American Academy of Pediatrics has recommended an oseltamivir treatment dose of 3.5 mg/kg orally twice daily for infants 9-11 months old, on the basis of data which indicated that a higher dose of 3.5 mg/kg was needed to achieve the protocol-defined targeted exposure for this cohort as defined in the CASG 114 study (Kimberlin, 2013). It is unknown whether this higher dose will improve efficacy or prevent the development of antiviral resistance. However, there is no evidence that the 3.5 mg/kg dose is harmful or causes more adverse events to infants in this age group.

[4] Current weight-based dosing recommendations are not appropriate for premature infants. Premature infants might have slower clearance of oral oseltamivir because of immature renal function, and doses recommended for full-term infants might lead to very high drug concentrations in this age group. CDC recommends dosing as also recommended by the American Academy of Pediatrics (Committee on Infectious Diseases, 2018): limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provide the basis for dosing preterm infants using their postmenstrual age (gestational age + chronological age): 1.0 mg/kg/dose, orally, twice daily, for those <38 weeks postmenstrual age; 1.5 mg/kg/dose, orally, twice daily, for those 38 through 40 weeks postmenstrual age; 3.0 mg/kg/dose, orally, twice daily, for those >40 weeks postmenstrual age.

[5] See Special Considerations for Institutional Settings section below for details regarding duration of chemoprophylaxis for outbreaks in institutional settings.

[6] Inhaled zanamivir is approved for treatment of acute uncomplicated influenza within 2 days of illness onset with twice-daily dosing in people 7 years and older, and for chemoprophylaxis with once-daily dosing in people 5 years and older.

[7] Intravenous peramivir is approved for treatment of acute uncomplicated influenza within 2 days of illness onset with a single dose in people 2 years and older. Daily dosing for a minimum of 5 days was used in clinical trials of hospitalized patients with influenza (de Jong, 2014, Ison, 2014).

[8] There are no data for use of peramivir or baloxavir for chemoprophylaxis of influenza.

[9] Oral baloxavir marboxil is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 12 years and older who are otherwise healthy, or at high risk of developing influenza-related complications. (Baloxavir marboxil [Xofluza] package insert). U.S. Food and Drug Administration website; 2019). Baloxavir marboxil should not be administered with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc); co-administration with polyvalent cation-containing products may decrease plasma concentrations of baloxavir which may reduce efficacy. There are no available published data from clinical trials for baloxavir treatment of influenza in patients who are pregnant, immunocompromised, have severe disease, or in hospitalized patients. A randomized clinical trial of baloxavir treatment of influenza in hospitalized patients 12 years and older is in-progress.

Table 3. Recommended Oseltamivir and Peramivir Dose Adjustments for Treatment or Chemoprophylaxis of Influenza in Adults with Renal Impairment or End Stage Renal Disease (ESRD) on Dialysis*†

Creatinine Clearance		Recommended Treatment Regimen	Recommended Chemoprophylaxis Regimen
Oral oseltamivir[1]	Creatinine clearance 61 to 90 mL/min	75 mg twice a day	75 mg once daily
	Creatinine clearance 31 to 60 mL/min	30 mg twice a day	30 mg once daily
	Creatinine clearance 11 to 30 mL/min	30 mg once daily	30 mg every other day
	ESRD Patients on Hemodialysis Creatinine clearance ≤10 mL/min	30 mg after every hemodialysis cycle. Treatment duration not to exceed 5 days[2]	30 mg after alternate hemodialysis cycles[3]
	ESRD Patients on Continuous Ambulatory Peritoneal Dialysis[4] Creatinine clearance ≤10 mL/min	A single 30 mg dose administered immediately after a dialysis exchange	30 mg once weekly immediately after dialysis exchange
Intravenous Peramivir (single dose)[5]	Creatinine clearance ≥50 mL/min	600 mg	N/A
	Creatinine clearance 30 to 49 mL/min	200 mg	N/A
	Creatinine clearance 10 to 29 mL/min	100 mg	N/A
	ESRD Patients on Hemodialysis	Dose administered after dialysis at a dose adjusted based on creatinine clearance	

Abbreviations: N/A = not applicable

† From package inserts for oseltamivir and peramivir; see FDA Influenza (Flu) Antiviral Drugs and Related Information.

[1] Renal dosing of oseltamivir is not available in the package insert for pediatric patients. However, these tables may be useful for children who qualify for adult doses based on weight >40 kg.

[2] Assuming 3 hemodialysis sessions are performed in the 5- day period. Treatment can be initiated immediately if influenza symptoms develop during the 48 hours between hemodialysis sessions; however, the post-hemodialysis dose should still be administered independently of time of administration of the initial dose.

[3] An initial dose can be administered prior to the start of dialysis.

[4] Data derived from studies in continuous ambulatory peritoneal dialysis (CAPD) patients.

[5] Renal dosing from peramivir package insert is available for pediatric patients: Creatinine clearance ≥50 mL/min: 12 mg/kg (up to maximum dose of 600 mg); Creatinine clearance 30 to 49 mL/min: 4 mg/kg; Creatinine clearance 10 to 29 mL/min: 2 mg/kg.

***CDC. Influenza Antiviral Medications: Summary for Clinicians https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm**