PALTC PHARMACY

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New Influenza Drug Brings New Promise

Currently the Centers for Disease Control and Prevention (CDC) recommend that everyone 6 months of age and older receive a flu vaccine every season. Because the influenza virus replicates and mutates frequently, the vaccine often does not contain all the strains that people are infected with.

In long-term care facilities, an influenza outbreak is declared when two cases of laboratory-confirmed influenza are identified within 72 hours of each other in residents on the same unit. Outbreak control measures should be implemented as soon as possible. If one or more residents have acute respiratory illness and suspected influenza, control measures can be considered as soon as possible, even if the laboratory results are not yet available.

The 2018–2019 flu season is coming to an end, but an influenza outbreak can occur outside the normal flu season, although it is not commonly seen. Because of this, testing for influenza viruses and other respiratory illness pathogens should be performed during months outside the influenza season as well. If an outbreak occurs, health care professionals and facility staff need to ensure that standard and droplet precautions are followed for all residents with suspected or confirmed disease according to the CDC's guidance ("Prevention Strategies for Seasonal Influenza in Healthcare Settings," Oct. 20, 2018; http://bit.ly/2D73BXp).

For the 2018–2019 flu season, there are four antiviral drugs approved by the U.S. Food and Drug Administration and recommended by the CDC to treat influenza:

- Baloxavir marboxil (trade name Xofluza, approved 2018)
- Peramivir (trade name Rapivab, approved 2014)
- Oseltamivir phosphate (trade name Tamiflu, approved 1999), generic available
- Zanamivir (trade name Relenza, approved 1999)

Baloxavir marboxil (Xofluza)

Baloxavir marboxil is the newest agent approved for the treatment of acute uncomplicated influenza in patients 12 years of age and older. It is a polymerase acidic endonuclease inhibitor given as a single oral dose within 48 hours of the onset of symptoms with or without food, and it is dosed according to body weight.

Baloxavir is available as 20 mg and 40 mg tablets. Coadministration of dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids, or oral supplements such as calcium, iron, magnesium, selenium, or zinc is not recommended.

Patient Body Weight (kg)	Recommended Oral Dose
40 kg to <80 kg	Single dose of 40 mg
At least 80 kg	Single dose of 80 mg

The most common adverse reactions to baloxavir include diarrhea, bronchitis, nasopharyngitis, headache, and nausea. Baloxavir was not studied in patients older than 65. Also, there is no information on the stability of the tablets if they are crushed before administration, so the manufacturer does not recommend crushing the tablets.

Baloxavir has a different mechanism of action than the other currently recommended influenza antiviral drugs, which are neuraminidase inhibitors (NAIs). Given how frequently influenza viruses mutate and the potential for the viruses to develop resistance or reduced susceptibility to one or more influenza antiviral drugs, it is good to have other options for treating flu. This new drug could be useful if widespread resistance to the other influenza antiviral drugs is noted.

Peramivir (Rapivab)

Peramivir is an influenza virus NAI indicated for the treatment of acute uncomplicated influenza in patients 2 years old and older who have been symptomatic for no more than 2 days. It is given as a single infusion over 15 to 30 minutes, and it is available as a single-use vial containing 200 mg in 20 mL (10 mg/mL), which can be diluted with 0.9% or 0.45% sodium chloride, 5% dextrose, or lactated Ringer's solution to a maximum volume of 100 mL.

The adjustment of peramivir dosage for adults and adolescents aged 13 years and older with altered creatinine clearance (calculated using the Cockcroft–Gault equation) is as follows:

Clearance Creatinine	Single Dose
≥50 mL/minute	600 mg
30-49 mL/minute	200 mg
10-29 mL/minute	100 mg
Hemodialysis	Administer after dialysis

The clinical trials of peramivir did not include a sufficient number of individuals aged 65 and over to determine whether they respond differently than younger people. However, there have been no reported differences in exposures between older and younger individuals.

The most common adverse reactions to peramivir include diarrhea, anaphylaxis, serious skin/hypersensitivity reactions (i.e., Stevens-Johnson syndrome and erythema multiforme), and neuropsychiatric events. Peramivir is administered as an intravenous infusion and is only indicated for the treatment of influenza, so this medication is not recommended for prophylaxis of influenza in long-term care facilities.

Oseltamivir (Tamiflu)

Oseltamivir is a NAI indicated for the treatment of acute, uncomplicated influenza types A and B in patients 2 weeks old and older who have been symptomatic for less than 2 days. It is also indicated for influenza prophylaxis in patients 1 year old and older.

Oseltamivir is available as 30, 45, and 75 mg capsules. A 6 mg/mL suspension and dosing adjustments are recommended for patients with impaired renal function, including patients with end-stage renal disease (ESRD) and those on continuous ambulatory peritoneal dialysis (CAPD):

Adverse reactions to oseltamivir include nausea, vomiting, headache, serious skin/hypersensitivity reactions (i.e., Stevens-Johnson syndrome, toxic epidermal necrosis, and erythema), and neuropsychiatric events.

Clearance Creatinine	Recommended Treatment Dose	Recommended Prophylaxis Dose
>60 mL/minute	75 mg BID ×5 days	75 mg QD for at least 10 days
> 30-60 mL/minute	30 mg BID ×5 days	30 mg QD
>10-30 mL/minute	30 mg QD ×5 days	30 mg QOD
ESRD on hemodialysis	30 mg immediately then 30 mg after each dialysis cycle for no more than 5 days	30 mg immediately then 30 mg after alternate hemodialysis cycles
ESRD on CAPD	Single 30 mg dose	30 mg immediately then 30 mg once weekly

ESRD = end-stage renal disease; BID = twice daily; QD = once daily; QOD = every other day.

Zanamivir (Relenza)

Zanamivir is also an NAI that is indicated for the treatment of acute, uncomplicated influenza types A and B infections in patients age 7 and older who have had symptoms for less than 2 days. It is available as a dry powder inhaler with blister packs that contain the powder. Dosing for the treatment of influenza is 10 mg (two inhalations) twice daily for 5 days. Zanamivir has not been proven effective for influenza prophylaxis in nursing home residents.

No overall differences in safety or effectiveness have been observed between older and younger patients. However, elderly patients may need assistance with using the inhaler device. The adverse reactions to zanamivir include sinusitis, dizziness, fever and/or chills, arthralgia, and infectious arthritis.

Outbreak Prophylaxis

As soon as an influenza outbreak is confirmed, all residents on the same unit as a patient with active illness should be given chemoprophylaxis with an antiviral indicated for this use. Oseltamivir and zanamivir are the only two antivirals indicated for flu prophylaxis; if drug resistance to one

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EDITOR'S NOTE:

For the treatment of influenza, a full course of therapy ranges in price and is approximately the following, based on recent www.goodrx.com pricing (as of April 5, 2019). When comparing the prices of these agents, note that they will vary depending on dosage form, age, weight, renal function, and other factors for the patient.

- Baloxavir marboxil (Xofluza), $156
- Oseltamivir (generic Tamiflu, 30 and 75 mg capsules), $52
- Zanamivir (Relenza), $65
- Peramivir (Rapivab), $317

Many factors need to be considered before choosing the best therapy for an individual patient, but price alone should never be the reason for the final decision.

— Karl Steinberg, MD, CMD, HMDC
Editor-in-Chief