



Pharmacy Column



William Simonson,
PharmD, BCGP, FASCP

Influenza treatment with antiviral medications

William Simonson, PharmD, BCGP, FASCP

Oregon State University, USA



If an individual has the misfortune of contracting the flu either because they were not vaccinated, or they contracted a flu strain that is resistant to the vaccine they received, an active case of the flu can be treated with one of a number of antiviral medications although it is important to point out that the availability of these medications should not detract from the importance of being vaccinated against the flu. Antivirals should be used as a second line should previously administered vaccination be ineffective.

Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is hospitalized; has severe, complicated or progressive illness; or is at higher risk for influenza complications regardless of whether they have previously been vaccinated. High-risk patients include individuals over age 65 and residents of nursing homes and long-term care facilities.²

Antiviral flu treatment also can be considered for any previously healthy, symptomatic outpatient not at high risk for influenza complications, who is diagnosed with confirmed or suspected influenza, on the basis of clinical judgment, if treatment can be initiated within 48 h of illness onset.²

Two antivirals, amantadine and rimantadine are not recommended to treat the flu due to high levels of antiviral resistance among circulating influenza A viruses.² Currently, four influenza antiviral medications approved by the FDA are recommended for use in the United States during the 2018–19 flu season. Three of these newer anti-influenza drugs are chemically-related neuraminidase inhibitors. Oseltamivir (Tamiflu®), is taken by mouth and zanamivir (Relenza®) is administered by oral inhalation. It should be noted that some patients may have difficulty using the zanamivir inhaler device.

Each of these products are administered twice daily for five days after the onset of flu symptoms. A third agent, peramivir (Rapivab®) is administered intravenously in one dose infused over 15 to 30 min. Oral oseltamivir is the recommended antiviral for patients with severe, complicated, or progressive illness who are not hospitalized, and for hospitalized influenza patients.²

It is recommended that antiviral therapy be started within two days of the start of flu symptoms. These antiviral drugs won't result in an immediate cure but they can lessen symptoms and shorten the time patients feel sick by about one day.³ Rapid diagnosis is important so antiviral therapy can be started. The most commonly used test is called a rapid influenza diagnostics test, which looks for substances (antigens) on a swab sample from the back of the nose or throat. These tests can provide results in about 15 min. However, results vary greatly and are not always accurate. Other more reliable tests are available but treatment can begin based on the presence of flu symptoms.³

In October, 2018 the U.S. Food and Drug Administration approved a new antiviral drug indicated for the treatment of acute uncomplicated influenza. Baloxavir marboxil (trade name Xofluza®) is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 h. Unlike the other antivirals for flu, Xofluza® interferes with viral RNA transcription and blocks virus replication.² US Food and Drug Administration commissioner Scott Gottlieb, MD stated "This is the first new antiviral flu treatment with a novel mechanism of action approved by the FDA in nearly 20 years. With thousands of people getting the flu every year, and many people becoming seriously ill, having safe and effective treatment alternatives is critical. This novel drug provides an important, additional treatment option."⁴

E-mail address: wsimonsonpharmd@gmail.com

Xofluza[®] was approved by the FDA based on two randomized controlled clinical trials involving almost 2000 patients. These trials were designed to study both safety and efficacy of the drug. Study participants were assigned to receive either Xofluza[®], a placebo, or another antiviral influenza drug within 48 h of first experiencing flu symptoms. It is of interest that none of the subjects in these two pivotal clinical trials were age 65 or older. However, other published and ongoing studies include subjects over the age of 65.

In both pivotal trials patients' flu symptoms were alleviated more quickly in those treated with Xofluza[®] compared to placebo. However, in one of the trials there was no difference in the time it took to alleviate flu symptoms in the subjects who received Xofluza[®] and those who received the other flu treatment. The most common adverse reactions in patients taking Xofluza[®] included diarrhea and bronchitis.

Xofluza[®] was granted priority review by the FDA which is reserved for products that would significantly improve the safety or effectiveness of treating, diagnosing or preventing a serious condition. A significant difference between Xofluza[®] and Tamiflu[®], the other oral influenza antiviral drug, is that the entire Xofluza[®] treatment is administered in a single oral dose.

Co-administration of polyvalent cation-containing products may decrease Xofluza[®] absorption which could possibly decrease the product's efficacy. Dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives or antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc) should be avoided when taking Xofluza[®].

As with all new drugs, we won't know how Xofluza[®] will fit into our armamentarium of therapeutic weapons against influenza until we gain experience with its use.

As noted above, recommended duration for flu treatment is 5 days for oral oseltamivir or inhaled zanamivir. A longer duration of daily dosing can be considered for patients who remain severely ill after 5 days of treatment but this extended therapy is only for oseltamivir or zanamivir.²

Intravenous peramivir or oral baloxavir are given only as a single dose and are not approved for extended dosing.

This article was originally published in the middle of the 2018–19 US flu season. Since it takes approximately two weeks for a flu vaccination to stimulate flu resistance it's not too late to vaccinate and get protection for the latter part of the 2018 - 2019 flu season.¹

It is possible that long-term care facilities and other communities of elderly will be faced with flu outbreaks and epidemics. Preparation for such events is paramount and this is where these influenza antivirals can play a role in preventing individuals from contracting the flu. This application is referred to as chemoprophylaxis.

Use of antiviral drugs for chemoprophylaxis of influenza is a key component of influenza outbreak control in institutions that house

residents at higher risk of influenza complications. While highly effective, antiviral chemoprophylaxis is not 100% effective in preventing influenza illness. All eligible residents in the entire long-term care facility (not just currently impacted wards or areas) should receive antiviral chemoprophylaxis as soon as an influenza outbreak is determined.

When at least 2 patients are ill within 72 h of each other and at least one resident has laboratory-confirmed influenza, the facility should promptly initiate antiviral chemoprophylaxis to all non-ill residents, regardless of whether they have previously received influenza vaccination. Priority should be given to residents living in the same unit or floor as an ill resident. However, since staff and residents may spread influenza to residents on other units, floors, or buildings of the same facility, all non-ill residents are recommended to receive antiviral chemoprophylaxis to prevent transmission and control influenza outbreaks.⁵

CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks, and continuing for at least 7 days after the last known case is identified. There are no data for use of peramivir or baloxavir for chemoprophylaxis of influenza.

Preparation for a flu outbreak is important including establishing systems for rapid diagnosis, ordering of antivirals and quick access to sufficient quantities of these products.

Use of these antivirals to prevent flu outbreaks is an involved subject that cannot be dealt with in detail in the limited space available here but the reader is referred to the informative CDC publication cited in reference #5 below for a detailed description and discussion of chemoprophylaxis in long-term care facilities.

References

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