STEPS

New Drug Reviews

Baloxavir Marboxil (Xofluza) for Influenza

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Baloxavir marboxil (Xofluza) is an antiviral medication with a novel mechanism that inhibits an influenza virus–specific enzyme necessary for viral gene transcription and prevents influenza A and B virus replication. Baloxavir is labeled for the treatment of acute uncomplicated influenza in patients 12 years and older who have been symptomatic for no more than 48 hours.

Drug	Dosage	Dose form	Cost*
Baloxavir marboxil (Xofluza)	Weight-based dosing: 40 mg or 80 mg taken one time	20-mg or 40-mg tablets	$155

*—Estimated retail price of one dose based on information obtained at https://www.goodrx.com (accessed October 28, 2019).

Safety

A significant safety concern about baloxavir is that as an antiviral medication, it has no action against bacterial infections. Bacterial superinfections may occur in patients already infected with influenza, and treating influenza with baloxavir will not prevent or treat any secondary bacterial infections. Patients taking this medication do not require monitoring. Baloxavir has not been studied in children younger than 12 years, adults older than 65 years, or pregnant or lactating women.

Tolerability

Baloxavir is well tolerated by most patients. Reported adverse effects include diarrhea (3%), bronchitis (2%), nasopharyngitis (1%), nausea (1%), and headache (1%). These rates are all equal to or less than the same effects from placebo.[1]

Effectiveness

Baloxavir has been studied in healthy patients and in those considered to be at high risk for influenza complications (e.g., patients with asthma, lung disease, heart disease, or morbid obesity).[1,2] Baloxavir has been compared with placebo and with the neuraminidase inhibitor, oseltamivir (Tamiflu), in two randomized controlled trials over two different influenza seasons (2015 to 2016 and 2016 to 2017) involving a total of 1,836 otherwise healthy patients with influenza symptoms for no more than 48 hours, most of whom had polymerase chain reaction (PCR)-confirmed influenza A (73% to 88%) or influenza B.[2] Influenza A subtypes were either H1N1 or H3N2, which are the two strains of influenza contained in the annual vaccine. Only 20% to 37% of enrolled patients had received influenza vaccination.[2] Compared with placebo, baloxavir will decrease the duration of symptoms of uncomplicated PCR-confirmed influenza in adults 20 to 64 years of age by 24 to 30 hours (50 to 54 hours of symptoms with baloxavir, $P < .001$, vs. 78 to 80 hours with placebo, $P < .001$), as well as in adolescent patients 12 to 19 years of age (54 hours of symptoms with baloxavir vs. 80 hours with placebo, $P < .001$).[1,2] The approximate one-day reduction in symptom duration is similar to that for patients with PCR-confirmed influenza who are taking oseltamivir.[2] The key symptoms are cough, sore throat, nasal congestion, headache, fever, myalgia, and fatigue.[1]

As with other antiviral therapies, baloxavir has not been shown to decrease hospitalizations or pneumonia risk.[3] Patient-oriented outcomes such as effect on work or school days lost due to illness are unknown. Baloxavir has not been studied to determine its relative effectiveness in patients with influenza-like illness, which is a more typical, real-world clinical scenario. Based on previous studies of oseltamivir, limiting outcome reporting to patients with PCR-confirmed influenza will inflate the magnitude of benefit compared with patients who have influenza-like illness.[3]

Baloxavir is currently being assessed as a chemoprophylactic agent for patients exposed to influenza but not yet infected. Unpublished data show that a preventive dose of baloxavir taken after household exposure to influenza significantly reduces the likelihood of symptom development compared with placebo (1.9% vs. 13.6%, $P < .0001$). Approval for this indication has not been granted to date.[4] Unlike oral

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oseltamivir and inhaled zanamivir (Relenza), baloxavir is not recommended by the Centers for Disease Control and Prevention as a preventive treatment.

Price

A single dose of baloxavir (two tablets) costs approximately $155. This is significantly more expensive than oseltamivir, which costs about $50 for one course of treatment (10 capsules).

Simplicity

Baloxavir is taken once daily as a single dose of 40 mg (two tablets of 20 mg each) for patients weighing 88 to 176 lb (40 to 80 kg), or 80 mg (two tablets of 40 mg each) for patients weighing at least 176 lb (80 kg). Patients should take baloxavir within 48 hours of symptom onset. It should not be taken concurrently with calcium, iron, magnesium, antacids, dairy products, or calcium-fortified foods or beverages. It is unknown if baloxavir can be taken with live intranasal influenza vaccine.

Bottom Line

Single-dose baloxavir should be limited to ill patients who cannot tolerate or comply with a course of oseltamivir. For otherwise healthy adults with confirmed influenza or influenza-like illness, the high cost of baloxavir may not justify the one-day reduction in symptoms of a self-limited illness. Given its novel mechanism of action, baloxavir does have a theoretical role in potential future influenza seasons in which the virus may mutate and develop nonsusceptibility to existing antiviral neuraminidase inhibitors (which last occurred in 2009).[5,6] Unless further indications are approved, baloxavir should not be used in patients with influenza to limit infectivity or for prophylaxis in patients exposed to, but not infected with, influenza. Efforts should instead be invested in increasing vaccination rates and encouraging hand hygiene, over-the-counter analgesics, and other supportive care.

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