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The FDA Expands Indication for Baloxavir Marboxil to Include Post-Exposure Influenza Prevention

Announcer:
You're listening to The Drug Report on ReachMD, hosted by Linda Bernstein, Pharm.D., Clinical Professor on the Volunteer Faculty of the School of Pharmacy, University of California, San Francisco.

Dr. Bernstein:
Welcome to The Drug Report.

Baloxavir marboxil (brand name, Xofluza®) is an oral anti-influenza drug, the prodrug of baloxavir acid. It is characterized as a first-in-class, small molecule inhibitor of the polymerase acidic (PA) protein subunit of the influenza virus polymerase complex. Baloxavir (after conversion to baloxavir acid) acts to block influenza virus replication by inhibiting the cap-dependent endonuclease activity of the PA protein.

In 2018, the U.S. Food and Drug Administration approved Xofluza (baloxavir marboxil) for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours. Approval was granted to Shionogi & Co., Ltd.

The safety and efficacy of Xofluza, taken as a single oral dose, was demonstrated in two randomized controlled clinical trials of 1,832 patients where participants were assigned to receive either Xofluza, a placebo, or another antiviral flu treatment within 48 hours of experiencing flu symptoms. In both trials, patients treated with Xofluza had a shorter time to alleviation of symptoms compared with patients who took the placebo. In the second trial, there was no difference in the time to alleviation of symptoms between subjects who received Xofluza and those who received the other flu treatment.

The U.S. Food and Drug Administration expanded the approved indication for Xofluza (baloxavir marboxil) on November 23, 2020, to include post-exposure prevention of influenza for patients 12 years of age and older after contact with an individual who has the flu. Xofluza, previously available only in tablet form, is also now available as granules for mixing in water as a suspension for oral or enteral use.

Debra Birnkrant, M.D., director of the Division of Antiviral Products in the FDA's Center for Drug Evaluation and Research stated: "This expanded indication for Xofluza will provide an important option to help prevent influenza just in time for a flu season that is anticipated to be unlike any other because it will coincide with the coronavirus pandemic. Americans will have to be more vigilant than ever as these viruses spread concurrently."

Xofluza's safety and efficacy for post-influenza exposure prevention is supported by one randomized, double-blind, controlled trial in which 607 subjects, 12 years of age and older who were exposed to a person with influenza in their household, received either a single dose of Xofluza or a single dose of a placebo. Of these 607 subjects, 303 received Xofluza and 304 received the placebo. The trial's primary endpoint was the proportion of subjects who were infected with influenza virus and presented with fever and at least one respiratory symptom from day 1 to day 10. Of those who received Xofluza, 1% of subjects met these criteria, compared to 13% of subjects who received a placebo for the clinical trial.

The most common side effects of Xofluza include diarrhea, bronchitis, nausea, sinusitis and headache. In randomized clinical trials there was evidence of development of reduced susceptibility in some patients treated with baloxavir.

Hypersensitivity, including anaphylaxis (allergic reaction), can occur in patients taking Xofluza. Patients should not take Xofluza if they

have had a known hypersensitivity reaction to the drug. Xofluza should not be co-administered with dairy products, calcium-fortified beverages, or laxatives, antacids, or oral supplements containing calcium, iron, magnesium, selenium, aluminum or zinc.

The FDA granted the approval of Xofluza in this expanded indication to Genentech USA, Inc.

Here are some additional study highlights of recently published research about baloxavir.

A post marketing surveillance of more than 3000 patients studied the safety and efficacy of baloxavir marboxil for the treatment of influenza in Japanese clinical practice. The study published in July 2020 in the Journal of Infectious Disease and Chemotherapy involved 688 Japanese hospitals or clinics (from March 2018 to March 2019). They enrolled patients of any age with influenza A or B who received a single, weight-based dose of baloxavir. Adverse drug reactions (ADRs) were seen in 11.2% of 3094 patients during the 7-day observation period; the most common ADR was diarrhea (6.1%). ADRs were more common in children aged <12 years (14.1%) than in adults (10.0%). Almost all ADRs were non-serious. Median time to alleviation of symptoms was 2.5 days (overall, influenza A, and influenza B groups). Median time to resolution of fever was 1.5 days (overall, influenza A, and influenza B groups). Biphasic fever (i.e., increased temperature after previous fever resolution) was seen in 6.7% of patients overall and 28.6% of patients <6 years infected with influenza B, similar to rates published elsewhere with other influenza drugs and in untreated influenza. The authors concluded that the study suggests that baloxavir is well tolerated and effective regardless of patient age or influenza virus type.

The Lancet Infectious Diseases, October 2020 issue described a double-blind, placebo-controlled and oseltamivir-controlled trial in outpatients aged 12 years and older. The study found that single dose baloxavir has superior efficacy to placebo and similar efficacy to oseltamivir for ameliorating influenza symptoms in high-risk outpatients. The safety of baloxavir was similar to placebo. The authors stated that this study supports early therapy for patients at high risk of complications of influenza to speed clinical recovery and reduce complications. Both studies were funded by or involved employees of Shionogi.

For The Drug Report, I'm Pharmacist Dr. Linda Bernstein.

Announcer:
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