BlueCross BlueShield Federal Employee Program

# XOFLUZA
# (baloxavir marboxil)

## RATIONALE FOR INCLUSION IN PA PROGRAM

### Background

Xofluza (baloxavir marboxil) is a prodrug that is converted by hydrolysis to baloxavir, the active form that exerts anti-influenza virus activity. Baloxavir inhibits the endonuclease activity of the polymerase acidic (PA) protein, an influenza virus-specific enzyme in the viral RNA polymerase complex required for viral gene transcription, resulting in inhibition of influenza virus replication. Efficacy of Xofluza in patients who begin treatment after 48 hours of symptoms has not been established (1).

### Regulatory Status

FDA-approved indications: Xofluza is an influenza virus polymerase acidic (PA) endonuclease inhibitor indicated for: (1)

- Treatment of acute uncomplicated influenza in patients 5 years of age and older who have been symptomatic for no more than 48 hours and who are otherwise healthy or at high risk of developing influenza-related complications
- Post-exposure prophylaxis of influenza in patients 5 years of age and older following contact with an individual who has influenza

Limitations of Use: (1)

- Influenza viruses change over time, and factors such as the virus type or subtype, emergence of resistance, or changes in viral virulence could diminish the clinical benefit of antiviral drugs.
- Consider available information on influenza drug susceptibility patterns for circulating influenza virus strains when deciding whether to use Xofluza.

Persons at high risk of complications from influenza should be considered for antiviral therapy. There is data to suggest that the highest risk of both mortality and serious morbidity (e.g., hospitalization) occurs for severely immunocompromised patients (e.g., hematopoietic stem cell transplant patients) and very elderly (age >85 years). Residents of nursing homes and infants aged <24 months also have high hospitalization rates but lower case-fatality rates than do the other 2 groups (2).

Examples of persons at high risk of complications would be: (2)

- Unvaccinated infants aged 12-24 months
- Persons with asthma or other chronic pulmonary diseases, such as cystic fibrosis in children or chronic obstructive pulmonary disease in adults.
- Persons with hemodynamically significant cardiac disease
- Persons who have immunosuppressive disorders or who are receiving immunosuppressive therapy
- HIV-infected persons
- Persons with sickle cell anemia and other hemoglobinopathies
- Persons with diseases that require long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Persons with chronic renal dysfunction
- Persons with cancer
- Persons with chronic metabolic disease, such as diabetes mellitus
- Persons with neuromuscular disorders, seizure disorders, or cognitive dysfunction that may compromise the handling of respiratory secretions
- Adults aged >65 years
- Residents of any age of nursing homes or other long-term care institutions

The safety and effectiveness of Xofluza in pediatric patients less than 5 years of age for the treatment of acute uncomplicated influenza who are otherwise healthy, and in post-exposure prophylaxis of influenza have not been established. The safety and effectiveness of Xofluza in pediatric patients less than 12 years of age for the treatment of acute uncomplicated influenza who are at high-risk have not been established (1).

**Summary**

Xofluza (baloxavir marboxil) is a prodrug that is converted by hydrolysis to baloxavir, the active form that exerts anti-influenza virus activity. Baloxavir inhibits the endonuclease activity of the polymerase acidic (PA) protein, an influenza virus-specific enzyme in the viral RNA polymerase complex required for viral gene transcription, resulting in inhibition of influenza virus replication. Efficacy of Xofluza in patients who begin treatment after 48 hours of symptoms has not been established (1).

BlueCross BlueShield Federal Employee Program

# XOFLUZA
# (baloxavir marboxil)

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Xofluza while maintaining optimal therapeutic outcomes.

**References**


1. Xofluza. [package insert]. South San Francisco, CA: Genentech USA, Inc.; March 2024.
2. IDSA Seasonal Influenza in Adults and Children – Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America. Clin Infect Dis. (2009) 48 (8): 1003-1032. http://cid.oxfordjournals.org/content/48/8/1003.1/F3.expansion.html.