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Section:	Prescription Drugs	**Effective Date:**	October 1, 2025
Subsection:	Anti-infective Agents	**Original Policy Date:**	November 9, 2018
Subject:	Xofluza	**Page:**	1 of 5

Last Review Date: September 19, 2025

Xofluza

Description

Xofluza (baloxavir marboxil)

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).

Related policies
Relenza, Tamiflu

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xofluza may be considered **medically necessary** if the conditions indicated below are met.

Xofluza may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 5 years of age and older

Diagnoses

Patient must have the following:

1. Treatment of influenza
    a. Acute uncomplicated influenza
    b. Onset of symptoms within the previous 48 hours

    AND ONE of the following:
    a. High risk for complications
    b. Immunocompromised
    c. Resides in an institutional setting (e.g., long-term care facility)

2. Prophylaxis of influenza
    a. Patient has had contact with an individual who has influenza

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

Age 5 years of age and older

Quantity

Strength and Dosage Form	Quantity
40 mg tablet	4 tablets **OR**
80 mg tablet	2 tablets **OR**
30 mg packets*	2 packets **OR**
40 mg packets*	4 packets **OR**
40 mg/20 mL for oral suspension*****	4 bottles

This formulation is included in this policy but is not available on the market as of yet

Duration 12 months

Prior - Approval Limits

Treatment or Prophylaxis of Influenza

Quantity

Strength and Dosage Form	Quantity
40 mg tablet	2 tablets **OR**
80 mg tablet	1 tablet **OR**
30 mg packets*	1 packet **OR**
40 mg packets*	2 packets **OR**
40 mg/20 mL for oral suspension*****	2 bottles

This formulation is included in this policy but is not available on the market as of yet

Duration 1 month

Prior – Approval *Renewal* Limits

None

Rationale

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).

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.; May 2025.
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.

Policy History

Date	Action
November 2018	Addition to PA
March 2019	Annual review and reference update
December 2020	Annual review and reference update
January 2021	Addition of indication: prophylaxis of influenza. Removed requirement that patient must weigh at least 40kg. Added Xofluza for oral suspension to quantity charts
March 2021	Annual review
August 2021	Added 80 mg tablet to quantity charts per latest PI update
September 2021	Annual review and reference update
September 2022	Per PI update: reduced age requirement to 5 and older. Also removed 20mg tablet from quantity charts
December 2022	Annual review and reference update
June 2023	Annual review
June 2024	Annual editorial review and reference update. Updated FDA approvals section
June 2025	Annual review and reference update
July 2025	Per PI update, added 30 mg and 40 mg packets
September 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 19, 2025 and is effective on October 1, 2025.