Clinical Policy: Baloxavir Marboxil (Xofluza)

Reference Number: CP.PMN.185
Effective Date: 12.01.18
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Baloxavir marboxil (Xofluza®) is an antiviral polymerase acidic (PA) endonuclease inhibitor.

FDA Approved Indication(s)

Xofluza is indicated for:

- 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.

Limitation(s) of use: 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 drug susceptibility patterns for circulating influenza virus strains when deciding whether to use Xofluza.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Xofluza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Influenza Treatment and Post-Exposure Prophylaxis (must meet all)**:**

1. Request is for influenza treatment or post-exposure prophylaxis;
2. Age ≥ 5 years;
3. Member must use oseltamivir, unless one of the following applies (a, b, c, d, or e):
   a. Laboratory confirmation of influenza B infection (e.g., member, close contact);
   b. High prevalence of influenza B circulation in the community;
   c. Oseltamivir community resistance in the current influenza season;
   d. Prior oseltamivir administration in the current influenza season;
   e. Oseltamivir contraindications or history of clinically significant adverse effects;
4. For oral suspension requests, member is unable to swallow tablets, has difficulty swallowing tablets, or requires enteral administration;
5. Dose does not exceed one of the following (a, b, or c):
   a. Weight < 20 kg (i or ii):

i. Bottle (1 and 2):
   1) 2 mg/kg once;
   2) 1 bottle once;
ii. Packet – for weight ≥ 15 kg only (1 and 2):
   1) 30 mg once;
   2) 1 packet once;

b. Weight 20 kg to < 80 kg (i and ii):
   i. 40 mg once;
   ii. 1 tablet, 1 packet, or 1 bottle once;
c. Weight ≥ 80 kg (i and ii):
   i. 80 mg once;
   ii. 1 tablet, 2 packets, or 2 bottles once.

Approval duration: 4 weeks (one dose only)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Influenza Treatment and Post-Exposure Prophylaxis

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDC: Centers for Disease Control and Prevention
FDA: Food and Drug Administration
IDSA: Infectious Diseases Society of America
PA: polymerase acidic

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

oseltamivir (Tamiflu®)	Influenza Treatment[1]
	• Pediatrics*
	  ○ Infants, pre-term, and term: weight-based dosing ranging from 1 mg/kg to 3 mg/kg PO BID for 5 days
	  ○ Age 1 to 12 years: weight-based dosing ranging from 30 mg to 75 mg PO BID for 5 days
	• Adults and adolescents*
	  ○ Age ≥ 13 years: 75 mg PO BID for 5 days
	Influenza Prophylaxis[1]
	• Pediatrics*
	  ○ Age 3 months to 8 months: 3 mg/kg PO QD. Duration of therapy is dependent on the type of exposure.
	  ○ Age 9 months to 11 months: 3.5 mg/kg PO QD. Duration of therapy is dependent on the type of exposure.
		150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	○ Age 1 to 12 years: Weight-based dosing ranging from 30 mg to 75 mg PO QD for 10 days • Adults and adolescents* ○ Age ≥ 13 years: 75 mg PO QD for 10 days (7 days if pregnant) • Community outbreak* ○ Age 1 to 12 years: Weight-based dosing ranging from 30 mg to 75 mg PO QD for up to 6 weeks ○ Age ≥ 13 years: 75 mg PO QD for up to 6 weeks **See also CDC/IDSA, American Academy of Pediatrics, and American College of Obstetrics and Gynecologists influenza resources for guidance.* *[1] Oral oseltamivir phosphate is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older, and for chemoprophylaxis in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics.*	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): history of hypersensitivity to baloxavir marboxil or any of its ingredients
- Boxed warning(s): none reported

Appendix D: High Risk Factors for Developing Influenza-Related Complications
Per the Centers for Disease Control and Prevention, the following are health factors known to increase the risk of developing serious complications from influenza:
- Age ≥ 65 years
- Children younger than 2 years old
- Asthma
- Neurologic and neurodevelopment conditions
- Blood disorders (such as sickle cell disease)
- Chronic lung disease (such as chronic obstructive pulmonary disease [COPD] and cystic fibrosis)
- Endocrine disorders (such as diabetes mellitus)
- Heart disease (such as congenital heart disease, congestive heart failure and coronary artery disease)
- Kidney diseases
- Liver disorders
- Metabolic disorders (such as inherited metabolic disorders and mitochondrial disorders)

- People who are obese with a body mass index (BMI) of 40 kg/m^2 or higher
- People younger than 19 years old on long-term aspirin- or salicylate-containing medications.
- People with a weakened immune system due to disease (such as people with HIV or AIDS, or some cancers such as leukemia) or medications (such as those receiving chemotherapy or radiation treatment for cancer, or persons with chronic conditions requiring chronic corticosteroids or other drugs that suppress the immune system)
- People who have had a stroke
- Pregnant people and people up to 2 weeks after the end of pregnancy
- People who live in nursing homes and other long-term care facilities
- People from certain racial and ethnic minority groups are at increased risk for hospitalization with flu, including non-Hispanic Black persons, Hispanic or Latino persons, and American Indian or Alaska Native persons

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

Influenza treatment or post-exposure prophylaxis	Adults and pediatric patients ≥ 5 years:
	• Weight < 20 kg (oral suspension only):
	  ○ Bottles: 2 mg/kg PO once
	  ○ Packets (for weight 15 kg to < 20 kg only): 30 mg PO once
	• Weight 20 kg to < 80 kg (oral suspension [bottles or packets] or tablets): 40 mg PO once
	• Weight ≥ 80 kg (oral suspension [bottles or packets] or tablets): 80 mg PO once
	
	Xofluza oral suspension (bottles or packets) may be also administered via enteral feeding tube
		80 mg once

VI. Product Availability

- Tablets: 40 mg, 80 mg
- Oral suspension (bottle): 40 mg/20 mL (2 mg/mL; 20 mL bottle)
- Oral suspension (packets): 30 mg, 40 mg (in about 15-20 mL of drinking water)

VII. References

1. Xofluza Prescribing Information. South San Francisco, CA: Genentech, Inc.; May 2025. Available at: https://www.gene.com/download/pdf/xofluza_prescribing.pdf. Accessed June 11, 2025.
2. Tamiflu Prescribing Information. South San Francisco, CA: Genentech, Inc.; August 2019. Available at: https://www.gene.com/download/pdf/tamiflu_prescribing.pdf. Accessed July 17, 2024.

3. Centers for Disease Control and Prevention. Influenza antiviral medications: summary for clinicians. Available at: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm. Last reviewed December 8, 2023. Accessed July 31, 2024.
4. Centers for Disease Control and Prevention. People at high risk for flu complications. Available at: https://www.cdc.gov/flu/highrisk/index.htm. Last reviewed August 25, 2023. Accessed July 31, 2024.
5. Centers for Disease Control and Prevention. Weekly U.S. influenza surveillance report. Available at: https://www.cdc.gov/flu/weekly/index.htm. Updated July 26, 2024. Accessed July 31, 2024.
6. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. Clin Infect Dis. 2019;68(6):e1.
7. AAP Committee on Infectious Diseases. Recommendations for Prevention and Control of Influenza in Children, 2023–2024. Pediatrics. 2023;152(4):e2023063772
8. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia: an official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019. DOI: 10.1164/rccm.201908-1581ST.
9. Ison MG, Portsmouth S, Yoshida Y, et al. Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial. Lancet Infect Dis. June 8, 2020;20:1204-14.
10. Ikematsu H, Hayden FG, Kawaguchi K, et al. Baloxavir marboxil for prophylaxis against influenza in household contacts. NEJM. July 23, 2020;383(4):309-320.
11. Influenza in pregnancy: prevention and treatment. Committee Statement No. 7. American College of Obstetricians and Gynecologists. Obstet Gynecol 2024;143:1–7. Available at: https://www.acog.org/clinical/clinical-guidance/committee-statement/articles/2024/02/influenza-in-pregnancy-prevention-and-treatment. Accessed July 31, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: no significant changes; updated FDA Approved Indication section with revised indication to specify use in healthy or high risk patients; references reviewed and updated.	07.01.20	11.20
RT4: new indication (influenza post-exposure prophylaxis) and oral suspension formulation added with redirection to oral tablets unless unable to swallow; added HIM line of business; added minimum weight requirement per PI; added examples of acceptable medical justification for inability to use oseltamivir added in Appendix D; references reviewed and updated.	01.15.20	02.21
4Q 2021 annual review: no significant changes; revised “medical justification” to “must use” language and moved information in Appendix D to the criteria set; HIM.PHAR.21 revised to HIM.PA.154; RT4: added 80 mg tablets and removed 20 mg tablets per updated PI; references reviewed and updated.	06.28.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; RT4: updated to reflect pediatric expansion from age at least 12 years to age at least 5 years, removed requirement for weight ≥ 40 kgs, and added Appendix D with high risk factors; references reviewed and updated. Template changes applied to other diagnoses/indications.	08.15.22	11.22
4Q 2023 annual review: for Appendix B, added Tamiflu pediatric dosing for ages 2 weeks to less than 1 year to align with prescriber information; updated Appendix D to align with current CDC High Risk Factors; references reviewed and updated.	07.31.23	11.23
RT4: updated to reflect new pediatric expansion from at least 12 years of age to age at least 5 years for those who are high risk of developing influenza-related complications per PI; updated Tamiflu pediatric dosages in Appendix B as recommended by the CDC and the American Academy of Pediatrics; references reviewed and updated.	03.12.24	
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.31.24	11.24
RT4: added new dosage form, packets for oral suspension.	06.11.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.