# Clinical Policy: Baloxavir Marboxil (Xofluza)

Reference Number: CP.PMN.185
Effective Date: 12.01.18
Last Review Date: 11.21
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 12 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 12 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 ≥ 12 years;
3. Member weighs at least 40 kg;
4. 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;
5. For oral suspension requests, member is unable to swallow tablets, has difficulty swallowing tablets, or enteral administration is required;

6. Dose does not exceed one of the following (a or b):
   a. Weight 40 kg to < 80 kg: 40 mg (1 tablet or 1 bottle) once;
   b. Weight ≥ 80 kg: 80 mg (1 tablet or 2 bottles) once.

**Approval duration: 4 weeks (one dose only)**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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<br>• Pediatrics* | 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 BID for 5 days<br>• Adults and adolescents*<br>○ Age ≥ 13 years: 75 mg PO BID for 5 days<br>Influenza Prophylaxis<br>• Pediatrics*<br>○ Age 1 to 12 years: Weight-based dosing ranging from 30 mg to 75 mg PO QD for 10 days<br>• Adults and adolescents*<br>○ Age ≥ 13 years: 75 mg PO QD for 10 days<br>• Community outbreak*<br>○ Age 1 to 12 years: Weight-based dosing ranging from 30 mg to 75 mg PO QD for up to 6 weeks<br>○ Age ≥ 13 years: 75 mg PO QD for up to 6 weeks<br>_____<br>**See also CDC/IDSA influenza resources for guidance.* | |

*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

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Influenza treatment or post-exposure prophylaxis | Adults and adolescents ≥ 12 years:<br>Weight 40 kg to < 80 kg: 40 mg PO once<br>Weight ≥ 80 kg: 80 mg PO once | 80 mg once |

## VI. Product Availability

- Tablets: 40 mg, 80 mg
- Oral suspension: 40 mg/20 mL (2 mg/mL; 20 mL bottle)

## VII. References

1. Xofluza Prescribing Information. South San Francisco, CA: Genentech, Inc.; March 2021. Available at: https://www.gene.com/patients/medicines/xofluza. Accessed October 7, 2021.
2. Tamiflu Prescribing Information. August 2019. South San Francisco, CA: Genentech, Inc.; August 2019. Available at: https://www.gene.com/download/pdf/tamiflu_prescribing.pdf. Accessed July 2, 2021.
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. Page last updated May 6, 2021. Accessed July 2, 2021.

4. Centers for Disease Control and Prevention. People at high risk for flu complications. Available at: https://www.cdc.gov/flu/highrisk/index.htm. Page last reviewed June 11, 2021. Accessed July 2, 2021.
5. Centers for Disease Control and Prevention. Weekly U.S. influenza surveillance report. Available at: https://www.cdc.gov/flu/weekly/index.htm. Page last reviewed June 25, 2021. Accessed July 2, 2021.
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. 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.
8. 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.
9. 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.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 10.30.18 | 11.18 |
| 4Q 2019 annual review: no significant changes; references reviewed and updated. | 08.08.19 | 11.19 |
| Revised dose optimization of tablets in criteria. | 02.14.20 | |
| 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 |

**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.

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**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.