Clinical Policy: Baloxavir Marboxil (Xofluza)

Reference Number: ERX.NPA.105
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 tablets 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications In Section I
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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

oseltamivir (Tamiflu®)	Influenza Treatment
	• Pediatrics*
	  ○ 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
	• Pediatrics*
	  ○ 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
	• 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 influenza resources for guidance.*
		150 mg/day

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: Weight 40 kg to < 80 kg: 40 mg PO once 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
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 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	06.28.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
the criteria set; RT4: added 80 mg tablets and removed 20 mg tablets per updated PI; references reviewed and updated.		

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.