

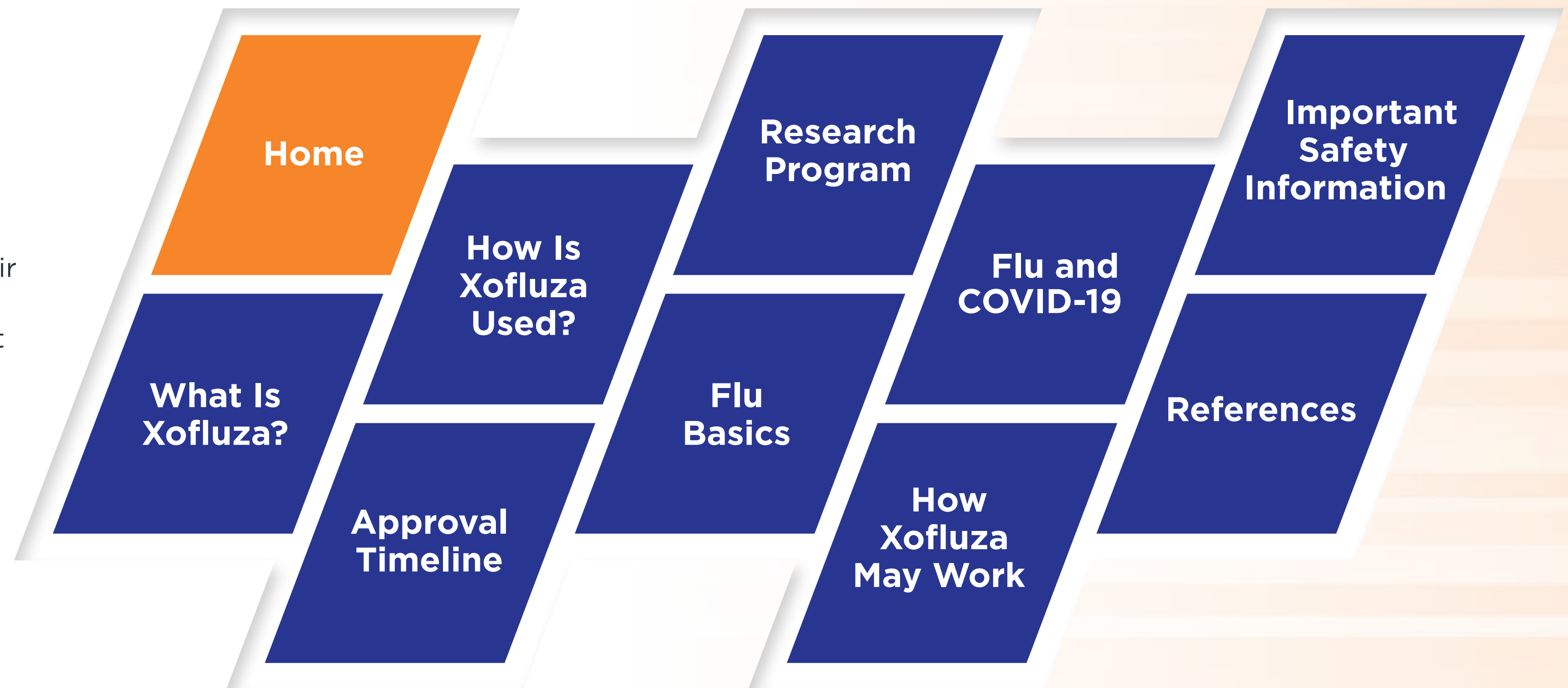


Continuing to advance the science and address critical needs in flu

This informational resource was developed as a reference guide for media only.

This resource details the clinical research program that has helped establish and expand the indications for Xofluza® (baloxavir marboxil), an FDA-approved antiviral medicine for use against influenza (flu). Use the tabs on the side of each page, and the links inside the text, for quick and easy access to information on Xofluza and the flu.

Media Inquiries:
(650) 467-6800





What is Xofluza?

Xofluza is approved by the U.S. Food and Drug Administration (FDA) as a single-dose, oral treatment for the flu (influenza) in people 12 years of age and older who have had flu symptoms for no more than 48 hours and who are otherwise healthy or at high risk of developing flu-related complications. It is also approved for post-exposure prophylaxis of flu in patients 12 years of age and older following contact with an individual who has the flu.¹

Key Phase III Study Results

CAPSTONE-1



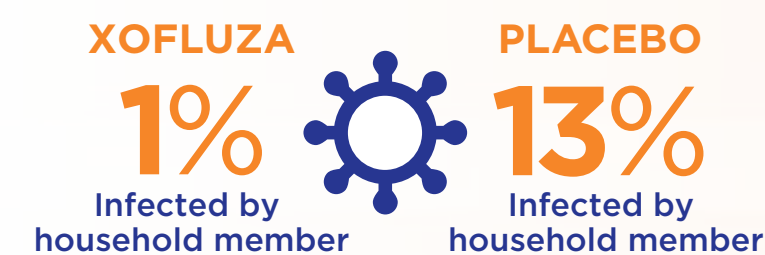
Xofluza significantly reduced the duration of flu symptoms compared to placebo (median time 54 hours versus 80 hours; $p < 0.001$) in patients aged 12 years and older. Similar efficacy results were seen between Xofluza and oseltamivir in relation to duration of symptoms (median time 54 hours versus 54 hours).^{1,2}

CAPSTONE-2



Xofluza significantly reduced the time to improvement of flu symptoms versus placebo in people age 12 years and older at high risk of complications from flu (median time 73 hours versus 102 hours; $p < 0.001$).^{1,10}

BLOCKSTONE



Xofluza showed a significant prophylactic effect compared with placebo in people aged 12 years and older following exposure to an infected household member. The proportion of household members who developed flu was 1% in participants treated with Xofluza and 13% in the placebo-treated group, demonstrating a 90% reduction in risk.^{1,11}



Xofluza is contraindicated in patients with a history of hypersensitivity to baloxavir marboxil or any of its ingredients. Serious allergic reactions have included anaphylaxis, angioedema, urticaria, and erythema multiforme.



First and Only single-dose, oral antiviral medicine to treat the flu^{1,4-6}



First and Only antiviral medicine indicated specifically for patients at high risk of developing serious complications from the flu^{1,3-6}



First single-dose antiviral medicine approved to help prevent flu in people who have been exposed to an individual who has the flu (known as post-exposure prophylaxis)^{1,4-6}



First FDA-approved medicine with a novel proposed mechanism of action to treat the flu in more than 20 years^{1,4-6}



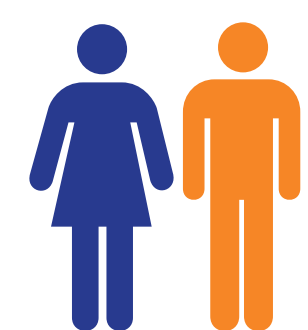
First antiviral medicine designed to inhibit the cap-dependent endonuclease protein within the flu virus, preventing the formation of new viral particles by blocking viral replication early in the flu lifecycle^{7,8}



First-in-Class medicine with demonstrated antiviral activity against a wide range of flu viruses, including oseltamivir-resistant strains and avian strains (H7N9, H5N1) in non-clinical studies^{1,9,*}

*The relationship between antiviral activity in cell culture and clinical response to treatment in humans has not been established.

M-US-00007626 (v2.0)



How is Xofluza Used?

Indications

Xofluza is a prescription medicine used to treat influenza (flu) in people 12 years of age and older who have had flu symptoms for no more than 48 hours and are otherwise healthy or at high risk of developing flu-related complications [see box at right]. It is also approved for post-exposure prophylaxis of flu in patients 12 years of age and older following contact with an individual who has the flu.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 drug susceptibility patterns for circulating influenza virus strains when deciding whether to use XOFLUZA.



The Centers for Disease Control and Prevention (CDC) defines people at high risk of serious flu complications as including those who have conditions such as asthma, chronic lung disease, diabetes, heart disease, and morbid obesity or adults 65 years of age or older. Access a full list at the web link above.³

Dosing¹



Tablets:
40 mg and
80 mg

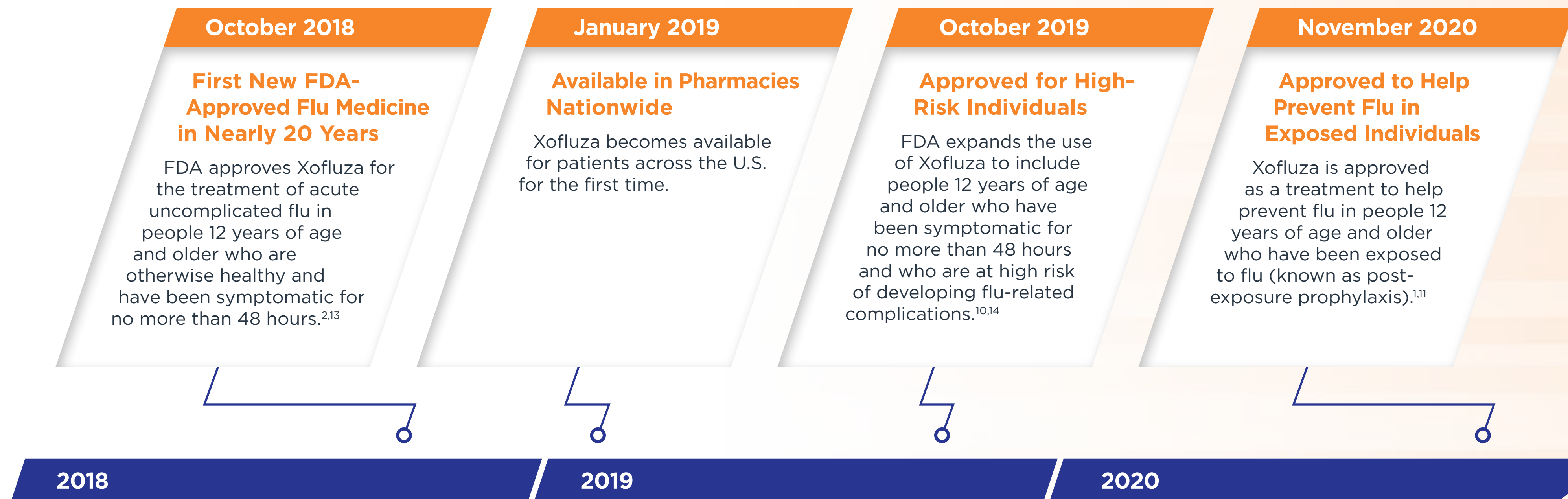
Based on results from clinical trials, **ONLY ONE DOSE** of Xofluza is needed to demonstrate benefit.

 Patient Body Weight (kg)	 Recommended Single Oral Dose in Patients 12 Years of Age and Older
<176 lbs (80 kg)	One 40-mg tablet (blister card contains one 40 mg tablet)
≥176 lbs (80 kg)	One 80-mg tablet (blister card contains one 80 mg tablet)

M-US-00007626 (v2.0)



Approval Timeline



M-US-00007626 (v2.0)



Research Program

Robust Clinical Evidence Demonstrates the Benefit of Xofluza in Different Populations and Treatment Settings

CAPSTONE-1 ^{1,2}	CAPSTONE-2 ^{1,10}	BLOCKSTONE ^{1,11}
Phase 1 2 3	Phase 1 2 3	Phase 1 2 3
Completion: 2018	Completion: 2019	Completion: 2020
Design 🔍 Multicenter, randomized, double-blind 🍷 Xofluza vs placebo vs oseltamivir	Design 🔍 Multicenter, randomized, double-blind 🍷 Xofluza vs placebo vs oseltamivir	Design 🔍 Multicenter, randomized, double-blind 🍷 Xofluza vs placebo
Patients (N=1436) 👤 Ages 12-64 ⚙️ Otherwise healthy with acute uncomplicated flu 🕒 Symptomatic for no more than 48 hours	Patients (N=2184) 👤 Ages 12+ ⚙️ At high risk of flu complications and having acute uncomplicated flu 🕒 Symptomatic for no more than 48 hours	Patients (N=607) 👤 Ages 12+ ⚙️ Individuals who are either otherwise healthy or at high risk of flu complications and are household contacts of patients with confirmed flu
Primary Endpoint Duration of symptoms (time to alleviation of symptoms) compared with placebo	Primary Endpoint Time to improvement of flu symptoms compared with placebo	Primary Endpoint Proportion of participants testing positive for flu, with fever and one or more respiratory symptoms
Across all studies, Xofluza was administered as a one-time weight-based dose; when used as a comparator, oseltamivir was administered as weight-based doses twice daily for 5 days.		

M-US-00007626 (v2.0)

Flu Basics

About Flu

Flu is a highly contagious illness caused by flu viruses that infect the nose, throat and sometimes the lungs. While flu viruses can be detected year-round in the U.S., they are most common during the fall and winter, with activity increasing in October and peaking between December and February. Some people are at higher risk for serious flu complications, including those who have conditions such as asthma, chronic lung disease, diabetes, heart disease and morbid obesity, and adults 65 years of age or older. For these people, contracting the flu puts them at higher risk of hospitalization or even death.^{3,15,18}

Flu Prevalence In The U.S.

Each year, up to 45 million people will be affected by the flu. Since 2010, the Centers for Disease Control and Prevention (CDC) estimates that the flu has resulted annually in^{16,17}


9.3M–45M
Illnesses


140K–810K
Hospitalizations


12K–61K
Deaths

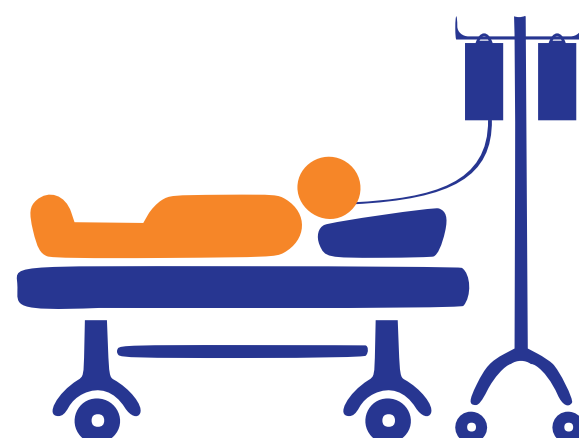
M-US-00007626 (v2.0)



Flu Prevention and Treatment During the COVID-19 Pandemic

The combination of a flu season and the global COVID-19 pandemic presents new challenges and unknowns. In addition to the added urgency for people to get a flu vaccine, FDA-approved antiviral treatments are available for those who contract the flu.^{1,4-6,12,18}

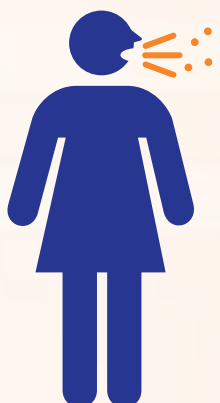
The CDC notes that flu and COVID-19 have overlapping signs and symptoms. During periods of community co-circulation of the two, the CDC cautions clinicians not to wait for the results of flu testing or SARS-CoV-2 testing before starting empiric antiviral treatment for flu in the following priority groups:¹²



Hospitalized patients with respiratory illness*



Outpatients with severe, complicated or progressive respiratory illness*



Outpatients at higher risk for flu complications who present with any acute respiratory illness symptoms (with or without fever)

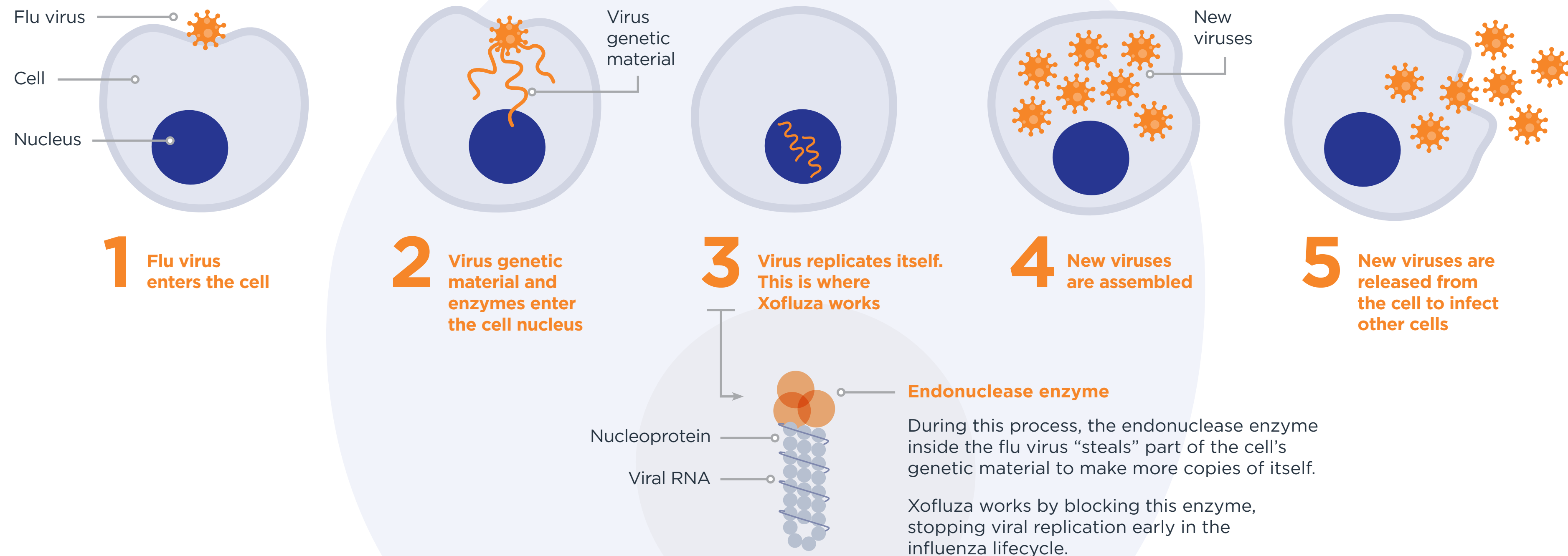
The CDC also noted that when influenza is known to be circulating in the community, clinicians can consider starting early (≤ 48 hours after illness onset) empiric antiviral treatment of non-high-risk outpatients with suspected flu based upon clinical judgment, including without an office visit. COVID-19 and other potential causes of symptoms should also be considered.¹²

*Xofluza is not indicated for these patient populations.

How Xofluza May Work

Xofluza is a single-dose, oral antiviral medicine that blocks an enzyme within the flu virus, stopping viral replication early in the flu lifecycle.^{1,7-9}

The Five Stages of the Flu Virus Lifecycle



M-US-00007626 (v2.0)

Important Safety Information¹

Xofluza U.S. Indication

XOFLUZA is a prescription medicine used to:

- Treat the flu (influenza) in people 12 years of age and older who have had flu symptoms for no more than 48 hours.
- Prevent the flu in people 12 years of age and older following contact with a person who has the flu.

It is not known if XOFLUZA is safe and effective in children less than 12 years of age.

Important Safety Information

Do not take XOFLUZA if you are allergic to baloxavir marboxil or any of the ingredients in XOFLUZA.

- Tell your healthcare provider about all of your medical conditions, including if you are:
 - Pregnant or plan to become pregnant. It is not known if XOFLUZA can harm your unborn baby.
 - Breastfeeding or plan to breastfeed. It is not known if XOFLUZA passes into your breast milk.
- Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, antacids, laxatives, vitamins, and herbal supplements.

Serious side effects may include

- Allergic reaction. Get emergency medical help right away if you develop any of the following signs or symptoms of an allergic reaction:
 - trouble breathing
 - skin rash, hives or blisters
 - swelling of your face, throat or mouth
 - dizziness or lightheadedness

The most common side effects of XOFLUZA in clinical studies were diarrhea, bronchitis, nausea, sinusitis, and headache. These are not all the possible side effects of XOFLUZA. Call your healthcare provider for medical advice about side effects.

XOFLUZA is not effective in treating or preventing infections other than influenza. Other kinds of infections can have symptoms like those of the flu or occur along with flu and may need different kinds of treatment. XOFLUZA does not prevent bacterial infections that may happen with the flu. Tell your healthcare provider if you feel worse or develop new symptoms during or after treatment with XOFLUZA or if your flu symptoms do not start to get better.

You are encouraged to report side effects to Genentech by calling 1-888-835-2555 or to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.

Please see full [Prescribing Information](#), including Patient Product Information.

M-US-00007626 (v2.0)

References

1. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2020.

2. Hayden FG, Sugaya N, Hirotsu N, et al. Baloxavir marboxil for uncomplicated influenza in adults and adolescents. *N Engl J Med*. 2018;379(10):913-923.

3. Centers for Disease Control and Prevention. People at High Risk For Flu Complications. <https://www.cdc.gov/flu/highrisk/index.htm>.

4. RAPIVAB [Prescribing information]. Durham, NC: BioCryst Pharmaceuticals, Inc. 2014.

5. RELENZA [Prescribing information]. Brentford, UK: GlaxoSmithKline; 1999.

6. TAMIFLU [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 1999.

7. Yuan S, Chu H, Singh K, et al. A novel small-molecule inhibitor of influenza A virus acts by suppressing PA endonuclease activity of the viral polymerase. *Scientific Reports*. 2016;6(1):22880.

8. Te Velthuis AJ, Fodor E. Influenza virus RNA polymerase: insights into the mechanisms of viral RNA synthesis. *Nature Reviews Microbiology*. 2016; 14(8):479-493.

9. Watanabe A, Hirotsu N, Ishida T, et al. Pharmacokinetic/pharmacodynamic analysis of S-033188, an influenza cap-dependent endonuclease inhibitor, from a phase 2, randomized, double-blind, placebo-controlled study in otherwise healthy adults with seasonal influenza. Presentation, 2017 European Congress of Clinical Microbiology & Infectious Diseases, Vienna, Austria.

10. 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*. 2020;20(10):1204-1214.

11. Ikematsu H, Hayden FG, Kawaguchi K, et al. Baloxavir marboxil for prophylaxis against influenza in household contacts. *N Engl J Med*. 2020;383(4):309-320.

12. Centers for Disease Control and Prevention. Influenza Antiviral Medications: Summary for Clinicians. <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. Updated August 31, 2020. Accessed September 14, 2020.

13. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2018.

14. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2019.

15. Centers for Disease Control and Prevention. About Flu. <https://www.cdc.gov/flu/about/index.html>. Updated September 12, 2019. Accessed September 14, 2020.

16. Centers for Disease Control and Prevention. Disease Burden of Influenza. <https://www.cdc.gov/flu/about/burden/index.html>. Updated April 17, 2020. Accessed September 14, 2020.

17. Centers for Disease Control and Prevention. Key Facts About Influenza (Flu). <https://www.cdc.gov/flu/keyfacts.htm>. Updated September 13, 2019. Accessed September 14, 2020.

18. Centers for Disease Control and Prevention. The Flu Season. <https://www.cdc.gov/flu/about/season/flu-season.htm>. Updated July 12, 2018. Accessed September 14, 2020.

M-US-00007626 (v2.0)