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 patients who have been symptomatic for no more than 48 hours and who are otherwise healthy adults and pediatric patients 5 years of age and older, or adults and pediatric patients 12 years of age and older who are at high-risk of developing flu-related complications. It is also approved for post-exposure prophylaxis of flu in patients 5 years of age and older following contact with an individual who has the flu.1

First and Only single-dose oral antiviral medicine to treat the flu in otherwise healthy adults and pediatric patients 5 years of age and older1,4-6

First and Only antiviral medicine indicated specifically for adults and pediatric patients 12 years of age and older who are at high-risk of developing flu-related complications1,3-6

First single-dose antiviral medicine approved to help prevent flu in people 5 years of age and older 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 years1,4-6

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 lifecycle7,8

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 studies9,10

Key Phase III Study Results

**CAPSTONE-1**

**XOFLUZA** 54 Hours

**PLACEBO** 80 Hours

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** 73 Hours

**PLACEBO** 102 Hours

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).1,2

**BLOCKSTONE**

**XOFLUZA** 2% Infected by household member

**PLACEBO** 13% Infected by household member

Xofluza showed a significant prophylactic effect compared with placebo in people aged 5 years and older following exposure to an infected household member. The proportion of household members who developed flu was 2% in participants treated with Xofluza and 13% in the placebo-treated group.1,3

**miniSTONE-2**

**XOFLUZA** 1 Dose (1 day)

**OSELTAMIVIR** 10 Doses (5 days, 2x a day)

A single oral dose of Xofluza showed comparable safety versus 10 doses of oseltamivir, taken twice daily for 5 days, in pediatric subjects (aged 5 to <12 years) who had flu-like symptoms but were otherwise healthy.1,3

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.

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

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**References**

1. 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

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).1,2

3. BLOCKSTONE. Xofluza showed a significant prophylactic effect compared with placebo in people aged 5 years and older following exposure to an infected household member. The proportion of household members who developed flu was 2% in participants treated with Xofluza and 13% in the placebo-treated group.1,3

4. miniSTONE-2. A single oral dose of Xofluza showed comparable safety versus 10 doses of oseltamivir, taken twice daily for 5 days, in pediatric subjects (aged 5 to <12 years) who had flu-like symptoms but were otherwise healthy.1,3

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How is Xofluza Used?

Indications

Xofluza is a prescription medicine used to treat influenza (flu) in patients who have been symptomatic for no more than 48 hours and who are otherwise healthy adults and pediatric patients 5 years of age and older, or adults and pediatric patients 12 years of age and older who are at high-risk of developing flu-related complications [see box right]. It is also approved for post-exposure prophylaxis of flu in patients 5 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.

Dosing¹

<table>
<thead>
<tr>
<th>Patient Body Weight (kg)</th>
<th>Recommended Single Oral Dose in Patients 5 Years of Age and Older (Tablets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 kg to less than 80 kg</td>
<td>One 40 mg tablet (blister card contains one 40 mg tablet)</td>
</tr>
<tr>
<td>At least 80 kg</td>
<td>One 80 mg tablet (blister card contains one 80 mg tablet)</td>
</tr>
</tbody>
</table>

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

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
First New FDA-Approved Flu Medicine in Nearly 20 Years

FDA approves Xofluza for the treatment of acute uncomplicated flu in people 12 years of age and older who are otherwise healthy and have been symptomatic for no more than 48 hours.2,14

Available in Pharmacies Nationwide

Xofluza becomes available for patients across the U.S. for the first time.

Approved for High-Risk Individuals

FDA expands the use of Xofluza to include people 12 years of age and older who have been symptomatic for no more than 48 hours and who are at high risk of developing flu-related complications.10,16

Approved to Help Prevent Flu in Exposed Individuals

Xofluza is approved as a treatment to help prevent flu in people 12 years of age and older who have been exposed to flu (known as post-exposure prophylaxis).17

Approved to Treat Pediatric Patients 5 Years of Age and Older

FDA approved Xofluza for the treatment of acute uncomplicated influenza in otherwise healthy children aged 5 to less than 12 years of age who have been symptomatic for no more than 48 hours. Xofluza was also approved for post-exposure prophylactic use in the same age group.18

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

**CAPSTONE-1**
- **Phase**: 1, 2, 3
- **Completion**: 2018
- **Design**: Multicenter, randomized, double-blind
  - Xofluza vs placebo vs oseltamivir
- **Patients** (N=1436)
  - Ages 12–64
  - Otherwise healthy with acute uncomplicated flu
  - Symptomatic for no more than 48 hours
- **Primary Endpoint**: Duration of symptoms (time to alleviation of symptoms) compared with placebo

**CAPSTONE-2**
- **Phase**: 1, 2, 3
- **Completion**: 2019
- **Design**: Multicenter, randomized, double-blind
  - Xofluza vs placebo vs oseltamivir
- **Patients** (N=2182)
  - Ages 12+
  - At high risk of flu complications and having acute uncomplicated flu
  - Symptomatic for no more than 48 hours
- **Primary Endpoint**: Time to improvement of flu symptoms compared with placebo

**BLOCKSTONE**
- **Phase**: 1, 2, 3
- **Completion**: 2020
- **Design**: Multicenter, randomized, double-blind
  - Xofluza vs placebo
- **Patients** (N=715)
  - Ages 5+
  - Individuals who are either otherwise healthy or at high risk of flu complications and are household contacts of patients with confirmed flu
- **Primary Endpoint**: Proportion of participants testing positive for flu, with fever and one or more respiratory symptoms

**miniSTONE-2**
- **Phase**: 1, 2, 3
- **Completion**: 2020
- **Design**: Multicenter, randomized, double-blind
  - Xofluza vs oseltamivir
- **Patients** (N=118)
  - Ages 5 to < 12 years of age
  - Otherwise healthy with confirmed symptomatic influenza
  - Symptomatic for no more than 48 hours
- **Primary Endpoint**: Adverse events or severe adverse events up to 29 days of follow-up

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.
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.3,6,19

Flu Prevalence In The U.S.
From 2010 to 2020, the Centers for Disease Control and Prevention (CDC) estimates that the flu has resulted annually in

<table>
<thead>
<tr>
<th>Illnesses</th>
<th>Hospitalizations</th>
<th>Deaths</th>
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<tbody>
<tr>
<td>9M–41M</td>
<td>140K–710K</td>
<td>12K–52K</td>
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References
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.1,4-6,13,19 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:13

- **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.13

*Xofluza is not indicated for these patient populations.
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

1. Flu virus enters the cell
2. Virus genetic material and enzymes enter the cell nucleus
3. Virus replicates itself. This is where Xofluza works
4. New viruses are assembled
5. New viruses are released from the cell to infect other cells

During this process, the endonuclease enzyme inside the flu virus "steals" part of the cell’s genetic material to make more copies of itself. Xofluza works by blocking this enzyme, stopping viral replication early in the influenza lifecycle.
What is XOFLUZA?

XOFLUZA is a prescription medicine used to:

• Treat the flu (influenza) in people who have flu symptoms for no more than 48 hours and who are:
  - Otherwise healthy adults and children 5 years of age and older, or
  - Adults and children 12 years of age and older who are at high risk of developing problems from the flu.
• Prevent the flu in people 5 years of age and older following contact with a person who has the flu (post-exposure prophylaxis).

XOFLUZA does not treat or prevent illness that is caused by infections other than the influenza virus.

XOFLUZA does not prevent bacterial infections that may happen with the flu.

It is not known if XOFLUZA is safe and effective for the treatment and prevention of the flu in children less than 5 years of age. XOFLUZA is not for use in children less than 5 years of age.

Important Safety Information

Who should not take XOFLUZA?

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

What should I tell my healthcare provider before using 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.
• Talk to your healthcare provider before you receive a live flu vaccine after taking XOFLUZA.
• Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, antacids, laxatives, vitamins, and herbal supplements.

What are the possible side effects of XOFLUZA?

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 for treatment of the flu in adults and adolescents (12 years of age and older) were diarrhea, bronchitis, nausea, sinusitis, and headache.

The most common side effects of XOFLUZA for treatment of the flu in children (5 years of age to less than 12 years of age) were diarrhea and vomiting.

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. 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.
References


