

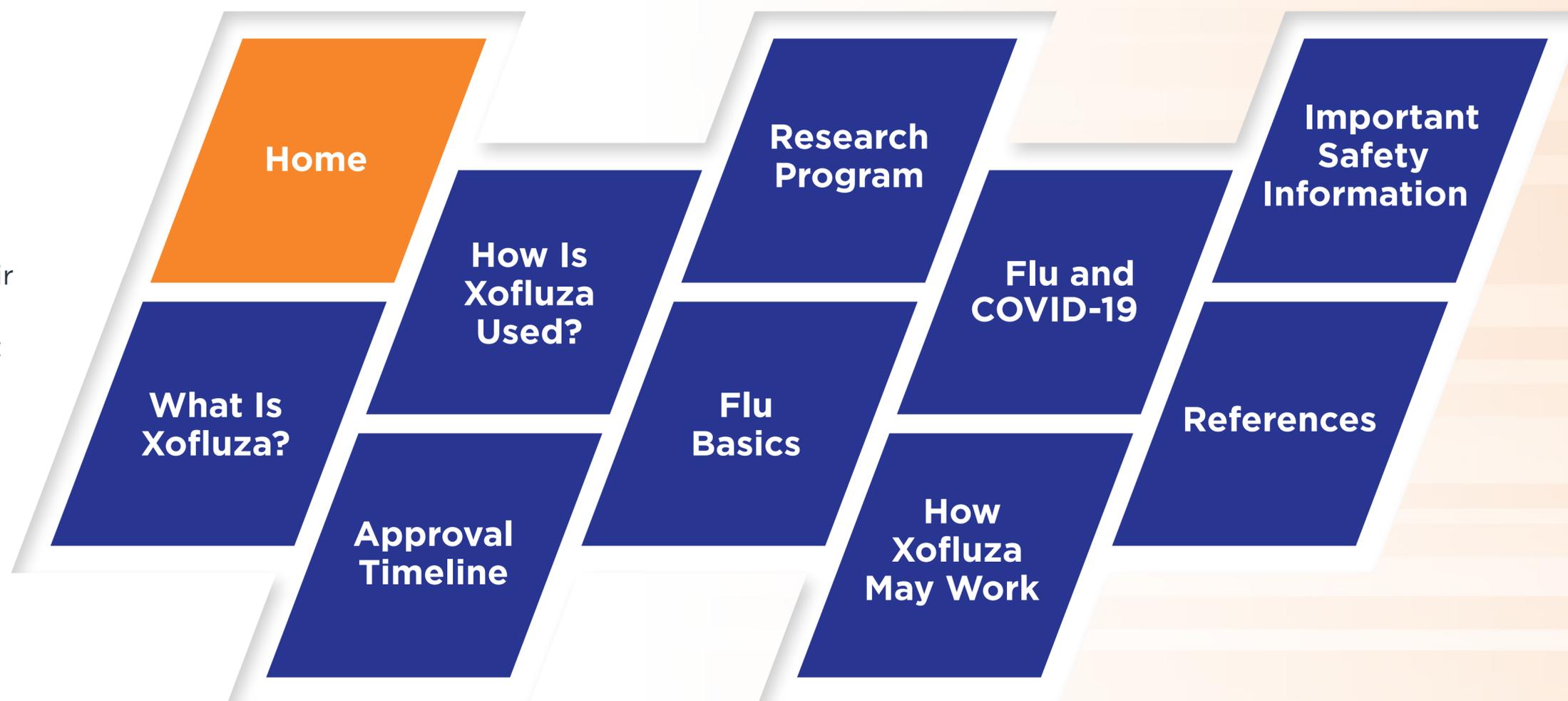


Continuing to advance the science and address critical needs in flu

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.

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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

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 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.^{1,11}

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.^{1,12}

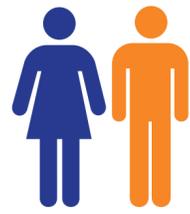


Xofluza is contraindicated in patients with a history of hypersensitivity to baloxavir marboxil or any of its ingredients. Serious allergic reactions have included anaphylaxis, angioedema, urticaria, and erythema multiforme.

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

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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



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 5 Years of Age and Older (Tablets)
20 kg to less than 80 kg	One 40 mg tablet (blister card contains one 40 mg tablet)
At least 80 kg	One 80 mg tablet (blister card contains one 80 mg tablet)

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

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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}	miniSTONE-2 ^{1,12}
Phase 1 2 3	Phase 1 2 3	Phase 1 2 3	Phase 1 2 3
Completion: 2018	Completion: 2019	Completion: 2020	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	Design Multicenter, randomized, double-blind Xofluza vs oseltamivir
Patients (N=1436) Ages 12-64 Otherwise healthy with acute uncomplicated flu Symptomatic for no more than 48 hours	Patients (N=2182) Ages 12+ At high risk of flu complications and having acute uncomplicated flu Symptomatic for no more than 48 hours	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	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 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	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.

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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.^{3,16,19}

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^{17,18}



9M-41M
Illnesses

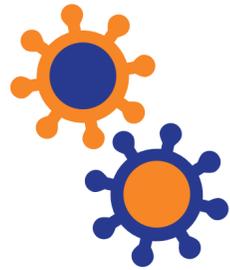


140K-710K
Hospitalizations



12K-52K
Deaths

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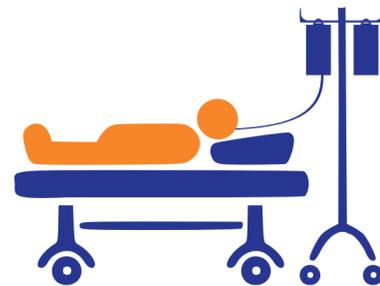


Flu and COVID-19

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.^{1,4-6,13,19}

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*



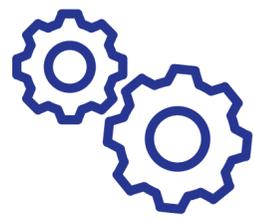
Outpatients at higher risk for flu complications who present with any acute respiratory illness symptoms (with or without fever)

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.

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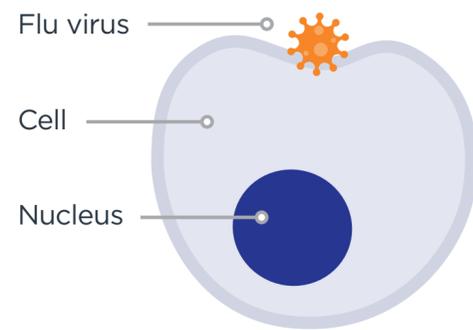




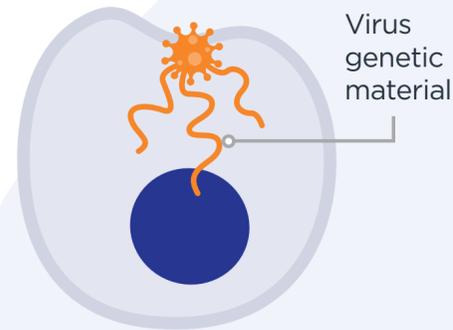
How Xofluza May Work

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



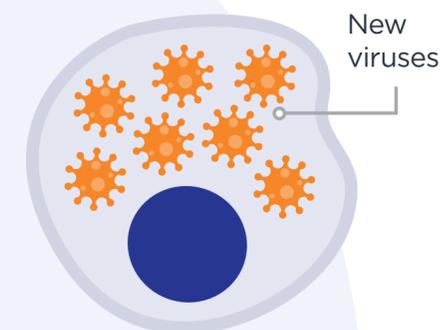
1 Flu virus enters the cell



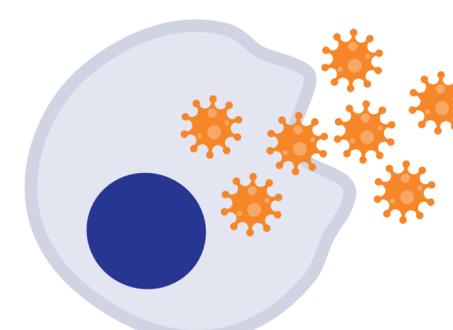
2 Virus genetic material and enzymes enter the cell nucleus



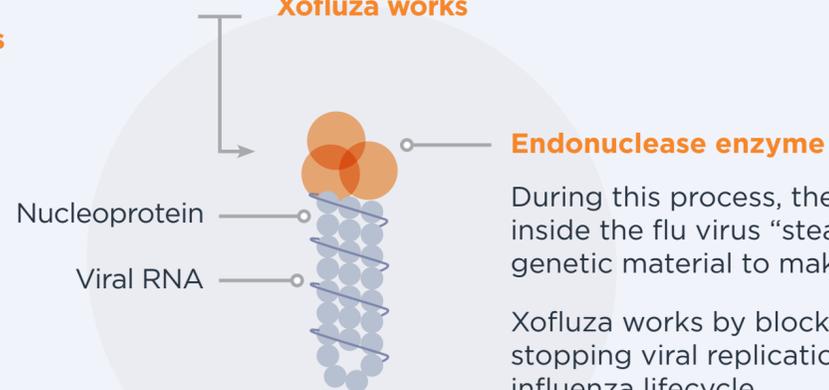
3 Virus replicates itself. This is where Xofluza works



4 New viruses are assembled



5 New viruses are released from the cell to infect other cells



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Important Safety Information¹

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.

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References

1. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2022.
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. 2021.
5. RELENZA [Prescribing information]. Brentford, UK: GlaxoSmithKline; 2021.
6. TAMIFLU [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2019.
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. Publication pending. Clinical trial currently available at US National Library of Medicine. <https://clinicaltrials.gov/ct2/show/NCT03629184>
13. 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.
14. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2018.
15. Xofluza [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc.; 2019.
16. Centers for Disease Control and Prevention. About Flu. <https://www.cdc.gov/flu/about/index.html>. Updated September 12, 2019. Accessed September 14, 2020.
17. Centers for Disease Control and Prevention. Disease Burden of Influenza. <https://www.cdc.gov/flu/about/burden/index.html>. Updated January 7, 2022. Accessed July 30, 2022.
18. Centers for Disease Control and Prevention. Key Facts About Influenza (Flu). <https://www.cdc.gov/flu/keyfacts.htm>. Updated September 13, 2019. Accessed July 30, 2022.
19. Here it isCenters for Disease Control and Prevention. What is Influenza (Flu)? <https://www.cdc.gov/flu/about/keyfacts.htm>. Updated August 26, 2021. Accessed August 16, 2022.

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