
1 DOSE
2.3 DAYS TO RELIEF
TELL THE FLU
ITS TIME IS UP
Introducing XOFLUZA, a 1-dose oral antiviral that shortens flu symptoms to just 2.3 days[1]*
*Median time vs placebo.
Indication
XOFLUZA™ is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours.
Limitations of Use
Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness.
See full Important Safety Information on page 7. Please read the enclosed full Prescribing Information.
Genentech
A Member of the Roche Group
Now Approved
xofluza™
(baloxavir marboxil) tablets 20mg 40mg

XOFLUZA: *the first and only 1-dose oral antiviral for the flu*

- Just 1 dose of XOFLUZA puts patients on track to be over and done with the flu[1]
- All it takes is 1 dose of XOFLUZA to stop viral replication at its source[1]

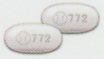
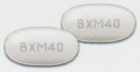
Now Approved **xofluza**™ (baloxavir marboxil) tablets

1 DOSE

oseltamivir

10 DOSES IN 5 DAYS

XOFLUZA tablets and oseltamivir capsules are shown at actual size.

Patient Body Weight	Recommended Oral Dose[1]
40 kg (88 lb) to less than 80 kg (176 lb)	1 dose of 40 mg  two 20-mg tablets (actual size)
At least 80 kg (176 lb)	1 dose of 80 mg  two 40-mg tablets (actual size)

Important Safety Information

Drug Interactions

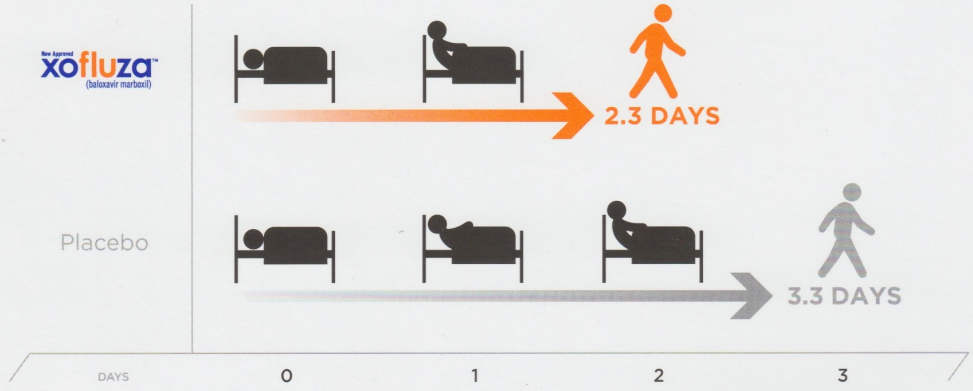
Co-administration with polyvalent cation-containing products may decrease plasma concentrations of baloxavir, which may reduce XOFLUZA efficacy. Avoid co-administration of XOFLUZA with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives or antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc).

See full Important Safety Information on page 7. Please read the enclosed full Prescribing Information.

Now Approved xofluza™ (baloxavir marboxil)

XOFLUZA helps your patients feel better, faster—*by shortening flu symptoms to just 2.3 days*

SHORTENED SYMPTOMS 33% FASTER THAN PLACEBO[1]



MEDIAN TIME TO ALLEVIATION OF SYMPTOMS IN TRIAL 2 (DAYS)

In Trial 1, conducted in Japan, subjects aged 20-64 years received XOFLUZA 40 mg (n=100) or placebo (n=100). The median value of the primary endpoint of **time to alleviation of symptoms (TTAS)** with XOFLUZA was 50 hours (95% confidence interval [CI]: 45, 64) vs 78 hours (95% CI: 68, 89) with placebo (p=0.014). In Trial 2, conducted in US and Japan, subjects aged 12-19 years received either XOFLUZA (n=80) or placebo (n=38); subjects aged 20-64 years received either XOFLUZA (n=375), oseltamivir[2] (n=377), or placebo (n=192). In total, 455 subjects were treated with XOFLUZA, 230 with placebo, and 377 with oseltamivir. In subjects aged 12-64 years, the median value of the primary endpoint of **TTAS** with XOFLUZA was 54 hours (95% CI: 50, 59) vs 80 hours (95% CI: 73, 87) with placebo (p<0.001). TTAS in both Trial 1 and Trial 2 was defined as the time when all of 7 symptoms (cough, sore throat, nasal congestion, headache, feverishness, myalgia, and fatigue) had been assessed by the subject as none or mild for a duration of at least 21.5 hours.

In a secondary endpoint in Trial 2, in subjects aged 20-64 years, reduction of duration of flu symptoms was similar with XOFLUZA compared with oseltamivir.[1]

- In the primary endpoint in Trial 2, 1-dose XOFLUZA reduced duration of flu symptoms to just 2.3 days compared with 3.3 days with placebo[1]

In adolescent subjects, XOFLUZA shortened flu symptoms 42% faster

In Trial 2, for subjects aged 12-17 years, time to symptom alleviation was achieved 39 hours faster with XOFLUZA (n=63) when compared to placebo (n=27) (median time of 54 h [95% CI: 43, 81] vs 93 h [95% CI: 64, 118]).[1]

Concurrent Use with Live Attenuated Influenza Vaccine

The concurrent use of XOFLUZA with intranasal live attenuated influenza vaccine (LAIV) has not been evaluated. Concurrent administration of antiviral drugs may inhibit viral replication of LAIV and thereby decrease the effectiveness of LAIV vaccination. Interactions between inactivated influenza vaccines and XOFLUZA have not been evaluated.

The flu evolves—*an antiviral should too*

XOFLUZA has broad-spectrum activity against influenza A and B* viruses, including oseltamivir-resistant strains.[1†]

A/H1N1, A/H3N2, and influenza B viruses are expected to be the major circulating strains during the 2018-2019 flu season.[3]

- A/H1N1
- AVIAN TYPE A/H5N1
- A/H3N2
- AVIAN TYPE A/H7N9
- Type B Viruses
- A/H1N1 H275Y
- A/H3N2 E119V
- A/H5N1 H275Y
- A/H7N9 R292K
- Type B D198E

Now Approved
xofluza™
(baloxavir marboxil)

Consider available information on influenza virus types or subtypes and on drug susceptibility patterns for circulating influenza virus strains when deciding whether to use XOFLUZA.

*The number of subjects who received XOFLUZA at the recommended dose and who were infected with influenza type B virus was limited, including 24 subjects in Trial 1 and 38 subjects in Trial 2.

†Antiviral activity was determined against laboratory strains and clinical isolates in vitro. The relationship between antiviral activity and clinical response to treatment in humans has not been established.

Important Safety Information (cont'd)

Most Common Adverse Reactions

Adverse events (regardless of causality assessment) reported in at least 1% of adult and adolescent subjects (n=710) who received XOFLUZA at the recommended dose included diarrhea (3%), bronchitis (2%), nausea (1%), nasopharyngitis (1%), and headache (1%).

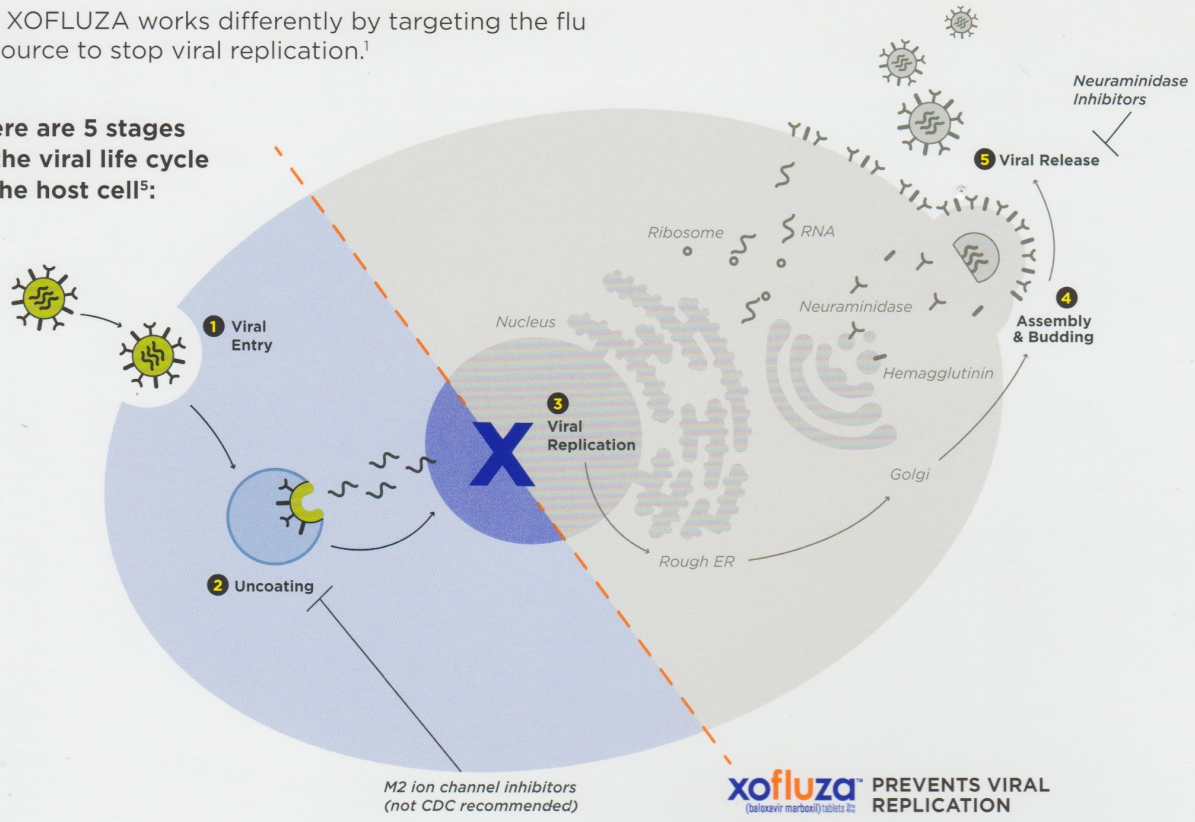
See full Important Safety Information on page 7.
Please read the enclosed full Prescribing Information.

Now Approved xofluza™ (baloxavir marboxil)

First-in-class XOFLUZA *stops the flu at its source*[1,4]

1-dose XOFLUZA works differently by targeting the flu at its source to stop viral replication.[1]

There are 5 stages of the viral life cycle in the host cell[5]:



- M2 ion channel blockers/adamantanes target viral uncoating in stage 2; however, they are no longer recommended by the CDC due to high resistance[4,6]
- Neuraminidase inhibitors (NAIs), such as oseltamivir, target the last stage of the viral life cycle: viral release. This prevents the already replicated virus from leaving the host cell[4,5]

***XOFLUZA works differently* by targeting the flu earlier at its source, in stage 3. XOFLUZA inhibits influenza-specific polymerase acidic endonuclease to prevent viral replication.[1,5]**

Indication

XOFLUZA™ is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

Limitations 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.

XOFLUZA *was as safe and well-tolerated as placebo**

XOFLUZA had a similar or lower adverse event rate than placebo across 2 clinical trials.[1]

INCIDENCE OF ADVERSE EVENTS OCCURRING IN ≥1% OF SUBJECTS RECEIVING XOFLUZA OR PLACEBO, IN THE ACUTE UNCOMPLICATED INFLUENZA TRIALS[1]

Adverse Event	XOFLUZA (n=710)	Placebo (n=409)
Diarrhea	3%	5%
Bronchitis	2%	4%
Nausea	1%	1%
Nasopharyngitis	1%	1%
Headache	1%	2%

The safety and efficacy of XOFLUZA have not been established in pediatric subjects under 12 years of age or weighing less than 40 kg.

*Based on combined Trial 1 and Trial 2 data, a total of 910 subjects received XOFLUZA: 834 (92%) were adults (aged ≥ 18 years) and 76 (8%) were adolescents (aged 12 to < 18 years). Of these, 710 subjects received XOFLUZA at the recommended dose.

Important Safety Information (cont'd)

Bacterial Infections

There is no evidence of efficacy of XOFLUZA in any illness caused by pathogens other than influenza viruses. Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as a complication of influenza. XOFLUZA has not been shown to prevent such complications. Prescribers should be alert to potential secondary bacterial infections and treat them as appropriate.

See full Important Safety Information on page 7. Please read the enclosed full Prescribing Information.

Now Approved
xofluza™
(baloxavir marboxil)

Indication

XOFLUZA™ is indicated for the treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 48 hours.

Limitations 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.

Important Safety Information

Bacterial Infections

There is no evidence of efficacy of XOFLUZA in any illness caused by pathogens other than influenza viruses. Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as a complication of influenza. XOFLUZA has not been shown to prevent such complications. Prescribers should be alert to potential secondary bacterial infections and treat them as appropriate.

Drug Interactions

Co-administration with polyvalent cation-containing products may decrease plasma concentrations of baloxavir, which may reduce XOFLUZA efficacy. Avoid co-administration of XOFLUZA with dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives or antacids, or oral supplements (e.g., calcium, iron, magnesium, selenium, or zinc).

Concurrent Use with Live Attenuated Influenza Vaccine

The concurrent use of XOFLUZA with intranasal live attenuated influenza vaccine (LAIV) has not been evaluated. Concurrent administration of antiviral drugs may inhibit viral replication of LAIV and thereby decrease the effectiveness of LAIV vaccination. Interactions between inactivated influenza vaccines and XOFLUZA have not been evaluated.

Most Common Adverse Reactions

Adverse events (regardless of causality assessment) reported in at least 1% of adult and adolescent subjects (n=710) who received XOFLUZA at the recommended dose included diarrhea (3%), bronchitis (2%), nausea (1%), nasopharyngitis (1%), and headache (1%).

For additional important safety information, please see XOFLUZA full prescribing information at **www.XOFLUZA.com.**

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.

REFERENCES: 1. XOFLUZA [Prescribing Information]. South San Francisco, CA: Genentech USA, Inc; 2018. **2.** Hayden FG, Sugaya N, Hirotsu N, et al; Baloxavir Marboxil Investigators Group. Baloxavir marboxil for uncomplicated influenza in adults and adolescents. *N Engl J Med.* 2018;379(10):913-923. Supplement available at: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1716197/suppl_file/nejmoa1716197_appendix.pdf. Accessed September 6, 2018. **3.** Garten R, Blanton L, Elal AIA, et al. Update: influenza activity in the United States during the 2017-18 season and composition of the 2018-19 influenza vaccine. *MMWR Morb Mortal Wkly Rep.* 2018;67(22):634-642. **4.** De Clercq E, Li G. Approved antiviral drugs over the past 50 years. *Clin Microbiol Rev.* 2016;29(3):695-747. **5.** von Itzstein M. The war against influenza: discovery and development of sialidase inhibitors. *Nat Rev Drug Discov.* 2007;6(12):967-974. **6.** Fiore AE, Fry A, Shay D, et al; Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2011;60(1):1-24.

TELL THE FLU ITS TIME IS UP

Introducing **XOFLUZA**, *a 1-dose oral antiviral that shortens flu symptoms to just 2.3 days*[1]*

- **Shortens flu symptoms to just 2.3 days**[1]*
- **Stops viral replication at its source**[1]
- **As safe and well-tolerated as placebo**[1]

*Median time vs placebo.

HELP YOUR PATIENTS *SAVE ON XOFLUZA*

Eligible patients may pay as little as $30.†
No activation required. Terms & Conditions apply.

LEARN MORE ABOUT XOFLUZA AND DOWNLOAD A COUPON AT XOFLUZA.COM/onedose

†Patient Eligibility/Terms and Conditions:

1. This offer is valid for eligible patients receiving prescription XOFLUZA. It may be used by those with or without commercial insurance, including patients who choose to pay cash. This offer may not be used for any other product.
2. **This offer may not be used by patients in conjunction with prescription insurance under Medicaid, Medicare, TRICARE or similar federal or state programs. This offer is not health insurance or a benefit plan.**
3. Offer only valid in the United States and U.S. Territories. This offer is not transferable and may not be combined with any other offer.
4. Offer must be presented along with a valid prescription for XOFLUZA at the time of purchase.
5. The patient or their guardian must be 18 years or older to receive coupon benefits.
6. May be used twice per season. **Valid until July 31, 2019**.
7. Coupon program is void where prohibited by law and on the date an AB rated generic equivalent for XOFLUZA becomes available.
8. Genentech USA, Inc. reserves the right to rescind, revoke, or amend this offer at any time without notice. It is a violation of federal law to buy, sell, or counterfeit this offer.

See additional Important Safety Information on page 7.
Please read the enclosed full Prescribing Information.

Genentech
A Member of the Roche Group

Now Approved
xofluza™
(baloxavir marboxil) tablets