CLINICAL UPDATE

Brand Name	Xofluza®
Generic Name	baloxavir marboxil
Drug Manufacturer	Genentech Inc

Clinical Update

TYPE OF CLINICAL UPDATE

New strength

FDA APPROVAL DATE

March 18, 2021

LAUNCH DATE

July 21, 2021

REVIEW DESIGNATION

Priority

TYPE OF REVIEW

New Drug Application (NDA): 210854

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Xofluza® is an influenza virus polymerase acidic (PA) endonuclease inhibitor 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.

MECHANISMS OF ACTION

Baloxavir marboxil is an oral prodrug that is converted to baloxavir, an inhibitor of the endonuclease activity of a selective polymerase acidic (PA) protein, which is required for viral gene transcription, resulting in inhibition of influenza virus replication. Baloxavir has demonstrated antiviral activity against influenza A and B viruses, including strains resistant to standard current antiviral agents.

DOSAGE FORM(S) AND STRENGTH(S)

- Tablets: 40 mg and 80 mg.
- For oral suspension: 40 mg/20 mL when constituted for final concentration of 2 mg/mL.

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DOSE & ADMINISTRATION

Treatment and Post-Exposure Prophylaxis of Influenza:
Xofluza® should be taken as a single dose as soon as possible and within 48 hours of influenza symptom onset for treatment of acute uncomplicated influenza or following contact with an individual who has influenza.
Xofluza® should be taken with or without food.

Patient Body Weight (kg)	Recommended Single Oral Dose in Patients 12 Years of Age and Older
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)

EFFICACY

Treatment of Acute Uncomplicated Influenza—Otherwise Healthy Subjects
Adults and Adolescents (Aged 12 Years and Older)
Two randomized, controlled, double-blinded clinical trials conducted in two different influenza seasons evaluated efficacy and safety of Xofluza® in otherwise healthy subjects with acute uncomplicated influenza.
In both trials, Xofluza® treatment at the recommended dose resulted in a statistically significant shorter time to alleviation of symptoms compared with placebo in the primary efficacy population.

Table- Time to Alleviation of Symptoms After Single Dose in Otherwise Healthy Adults with Acute Uncomplicated Influenza in Trial 1 (Median Hours)

	XOFLUZA 40 mg (95% CI[a]) N=100	Placebo (95% CI[a]) N=100
Adults (20 to 64 Years of Age)	50 hours[b] (45, 64)	78 hours (68, 89)

[a]CI: Confidence interval
[b]XOFLUZA treatment resulted in a statistically significant shorter time to alleviation of symptoms compared to placebo using the Gehan-Breslow's generalized Wilcoxon test (p-value: 0.014, adjusted for multiplicity using the Bonferroni method). The primary analysis using the Cox Proportional Hazards Model did not reach statistical significance (p-value: 0.165).

	XOFLUZA 40 mg or 80 mg (95% CI[a]) N=455	Placebo (95% CI[a]) N=230
Subjects (≥ 12 Years of Age)	54 hours[b] (50, 59)	80 hours (73, 87)

[a]CI: Confidence interval
[b]XOFLUZA treatment resulted in a statistically significant shorter time to alleviation of symptoms compared to placebo using the Peto-Prentice's generalized Wilcoxon test (p-value: < 0.001).

Treatment of Acute Uncomplicated Influenza—High Risk Subjects
Trial 3 (NCT02949011) was a randomized, double-blind, placebo- and active-controlled trial to evaluate the efficacy and safety of a single oral dose of Xofluza® compared with placebo or oseltamivir in adult and adolescent subjects 12 years of age or older with influenza who were at high risk of developing influenza related complications.

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Time to Improvement of Symptoms After Single Dose in High-Risk Subjects 12 Years of Age and Older with Acute Uncomplicated Influenza in Trial 3 (Median Hours)

XOFLUZA 40 mg or 80 mg[a] (95% CI[b]) N=385	Placebo (95% CI[b]) N=385
73 hours[c] (67, 85)	102 hours[c] (93, 113)

[a]The dosage of XOFLUZA was based on subject's weight.
[b]CI: Confidence interval
[c]XOFLUZA treatment resulted in a significant reduction in Time to Improvement of Influenza Symptoms compared to placebo using Peto-Prentice's generalized Wilcoxon test (p-value: < 0.001).