QUANTITY LIMIT CRITERIA

DRUG CLASS	**INFLUENZA TREATMENT & PREVENTION**
BRAND NAME* **(generic)**	**RELENZA (zanamivir)** **TAMIFLU (oseltamivir)** **XOFLUZA (baloxavir)**

Status: CVS Caremark Criteria
Type: Quantity Limit ***Ref # 110-H***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA APPROVED INDICATIONS

Relenza

Treatment of Influenza

Relenza (zanamivir) inhalation powder is indicated for treatment of uncomplicated acute illness due to influenza A and B virus in adults and pediatric patients aged 7 years and older who have been symptomatic for no more than 2 days.

Prophylaxis of Influenza

Relenza is indicated for prophylaxis of influenza in adults and pediatric patients aged 5 years and older.

Important Limitations of Use

Relenza is not recommended for treatment or prophylaxis of influenza in individuals with underlying airways disease (such as asthma or chronic obstructive pulmonary disease) due to risk of serious bronchospasm.

Relenza has not been proven effective for treatment of influenza in individuals with underlying airways disease.

Relenza has not been proven effective for prophylaxis of influenza in the nursing home setting.

Relenza is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control's Immunization Practices Advisory Committee.

Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Relenza.

There is no evidence for efficacy of zanamivir in any illness caused by agents other than influenza virus A and B.

Patients should be advised that the use of Relenza for treatment of influenza has not been shown to reduce the risk of transmission of influenza to others.

Compendial Uses

Treatment of influenza A or B viral infection when administered after 48 hours in patients aged 7 years and older who are at higher risk for influenza complications or in patients aged 7 years and older with severe, complicated, or progressive illness[4-8]

Tamiflu

Treatment of Influenza

Tamiflu is indicated for the treatment of acute, uncomplicated illness due to influenza A and B infection in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours.

Prophylaxis of Influenza

Tamiflu is indicated for the prophylaxis of influenza A and B in patients 1 year and older.
Limitations of Use
Tamiflu is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices.
Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Tamiflu.
Tamiflu is not recommended for patients with end-stage renal disease not undergoing dialysis.

Compendial Uses
Treatment of influenza A or B viral infection when administered after 48 hours in patients who are at higher risk for influenza complications or in patients with severe, complicated, or progressive illness[4-8]
Prophylaxis of influenza A or B viral infection in patients 3 months to 1 year of age if necessary after exposure to another person with influenza[4-8]

Xofluza
Treatment of Influenza
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 and who are: otherwise healthy, or at high risk of developing influenza-related complications.
Post-Exposure Prophylaxis of Influenza
Xofluza is indicated for post-exposure prophylaxis of influenza in persons 12 years of age and older following contact with an individual who has influenza.
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.

RATIONALE

The limits for Relenza and Tamiflu are based on the Center for Disease Control and Prevention (CDC) recommendation to allow a quantity to accommodate at least 2 weeks of community setting prophylaxis, at least 14 doses up to 20 doses (due to packaging), once every 90 days. The limits for Relenza and Tamiflu are also based on the recommended dosing regimen for the treatment or household prevention of influenza, providing quantity sufficient for 5 days of treatment or 10 days of household prevention, twice every 90 days, (10 doses each course for 2 courses, for a total of 40 blisters of Relenza, 20 capsules of Tamiflu 75mg or 45 mg, 40 capsules of Tamiflu 30mg [two capsules for 60mg dosing], or 6 bottles of Tamiflu suspension). The limits for Xofluza are based on the recommended dosing regimen for the treatment or post-exposure prophylaxis of influenza providing quantity sufficient for 1 day of therapy, twice every 90 days (1 dose each course for 2 courses, for a total of 2 tablets of the Xofluza 40mg (1 tablet per blister pack) or Xofluza 80mg (1 tablet per blister pack) or 4 tablets of Xofluza 20mg (2 tablets per blister pack) or Xofluza 40mg (2 tablets per blister pack) or 4 bottles of suspension).

If the patient is requesting more than the initial quantity limit, then the system will reject with a message indicating that a prior authorization is required. Quantities for extended community setting prophylaxis (Tamiflu, Relenza), or for another course of therapy for treatment (Tamiflu, Relenza, Xofluza), or household prevention/post-exposure prophylaxis (Tamiflu, Relenza, Xofluza) may be covered through the prior authorization.

The CDC states that influenza activity often begins to increase in October. Most of the time flu activity peaks between December and February, although activity can last as late as May.[6-8] When indicated, antiviral treatment should be started as soon as possible after illness onset, ideally within 48 hours of symptom onset.[6-8] The CDC states that antiviral treatment might have some benefits in patients with severe, complicated or progressive illness, and in patients at higher risk for influenza complications when started after 48 hours of illness onset.[4-8]

The CDC does not recommend widespread or routine use of antiviral medications for chemoprophylaxis so as to limit the possibilities that antiviral resistant viruses could emerge. To be effective as chemoprophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza and continued for 7 days after the

last known exposure. For persons taking antiviral chemoprophylaxis after inactivated influenza vaccination, the recommended duration is until immunity after vaccination develops (antibody development after vaccination takes about two weeks in adults and can take longer in children depending on age and vaccination history). For control of outbreaks in institutional settings (e.g. long-term care facilities for elderly persons and children) and hospitals, the CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks and continuing up to 1 week after the last known case was identified.[4-8]

Relenza (zanamivir)

Treatment

The recommended dose of Relenza for treatment of influenza in adults and pediatric patients aged 7 years and older is 10mg twice daily for 5 days.

Prophylaxis – Household

The recommended dose of Relenza for prophylaxis of influenza in adults and pediatric patients aged 5 years and older in a household setting is 10mg once daily for 10 days. There are no data on the effectiveness of prophylaxis with Relenza in a household setting when initiated more than 1.5 days after the onset of signs or symptoms in the index case.

Prophylaxis – Community

The recommended dose of Relenza for prophylaxis of influenza in adults and adolescents in a community setting is 10mg once daily for 28 days. There are no data on the effectiveness of prophylaxis with Relenza in a community outbreak when initiated more than 5 days after the outbreak was identified in the community. The safety and effectiveness of prophylaxis with Relenza have not been evaluated for longer than 28 days' duration.

The Relenza 10-mg dose is provided by 2 inhalations (one 5-mg blister per inhalation). Relenza is supplied in five Rotadisks each containing 4 blisters of the drug (20 blisters), packaged in a carton with 1 Diskhaler inhalation device.

Each dose of Relenza is provided by 2 inhalations, which is 2 blisters. Therefore, the initial limit will be 40 blisters, which allows for 20 doses of 2 inhalations per dose accommodating at least 14 doses up to 20 doses (due to packaging) for community prophylaxis, or 2 courses of therapy of 10 doses each for treatment or household prophylaxis, per 90 days.

Tamiflu (oseltamivir)

Treatment

The recommended oral dosage of Tamiflu for treatment of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) twice daily for 5 days.

The recommended oral dosage of Tamiflu for treatment of influenza in pediatric patients 2 weeks of age through 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for treatment in infants less than 2 weeks of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Prophylaxis - Household

Initiate post-exposure prophylaxis with Tamiflu within 48 hours following close contact with an infected individual. The recommended dosage of Tamiflu for prophylaxis of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) orally once daily for at least 10 days following close contact with an infected individual.

Prophylaxis in pediatric patients is recommended for 10 days following close contact with an infected individual. The recommended oral dosage of Tamiflu for prophylaxis of influenza in pediatric patients 1 year to 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for chemoprophylaxis in infants 3 months to 1 year of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Prophylaxis - Community

The recommended dosage of Tamiflu for prophylaxis of influenza in adults and adolescents 13 years and older is 75mg (one 75mg capsule or 12.5mL of oral suspension) orally once daily for up to 6 weeks during a community outbreak. In immunocompromised patients, Tamiflu may be continued for up to 12 weeks.

Prophylaxis in pediatric patients is recommended up to 6 weeks during a community outbreak. The recommended oral dosage of Tamiflu for prophylaxis of influenza in pediatric patients 1 year to 12 years of age is based on body weight, see table. Although not part of the FDA-approved indications, use of oral oseltamivir (Tamiflu) for chemoprophylaxis in infants 3 months to 1 year of age if necessary is recommended by the CDC and the American Academy of Pediatrics.[4-8]

Weight	Treatment Dosage for 5 days	Prophylaxis Dosage	Oral Suspension (6 mg/mL)	Bottles to Dispense	Capsules to Dispense (Strength)

		for 10 days	for each Dose		
Patients from 2 Weeks to less than 1 Year of Age					
Any weight	3mg/kg twice daily	Not applicable	0.5mL/kg	1 bottle	Not applicable
Patients 1 to 12 Years of Age Based on Body Weight					
15kg or less	30mg twice daily	30mg once daily	5mL	1 bottle	10 capsules (30mg)
15.1kg to 23kg	45mg twice daily	45mg once daily	7.5mL	2 bottles	10 capsules (45mg)
23.1kg to 40kg	60mg twice daily*	60mg once daily*	10mL	2 bottles	20 capsules (30mg)
40.1kg or more	75mg twice daily	75mg once daily	12.5mL	3 bottles	10 capsules (75mg)

*Two 30mg capsules should be used for the 60mg dose.

The Tamiflu dose is provided by 1 to 2 capsules or up to 12.5mL oral suspension based on age or body weight. Tamiflu capsules are available in 30mg, 45mg, and 75mg strengths in blister packs of 10. Tamiflu is also available as an oral suspension for constitution delivering 360mg/60mL (6mg/mL). Constituted oral suspension can be stored under refrigeration for up to 17 days or for up to 10 days at controlled room temperature.

Each dose of Tamiflu is provided by 1 to 2 capsules or up to 12.5mL oral suspension. Therefore, the initial limit will be 20 capsules of 45mg or 75mg, 40 capsules of 30mg (two capsules for 60mg dose), or 360mL of oral suspension, which allows for 20 doses, accommodating at least 14 doses up to 20 doses (due to packaging) for community prophylaxis, or 2 courses of therapy of 10 doses each for treatment or household prophylaxis, per 90 days.

Xofluza (baloxavir marboxil)

Treatment or Post-Exposure Prophylaxis

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. The recommended dosage of Xofluza in patients 12 years of age or older is a single weight-based dose as follows:

Recommended Xofluza Dosage in Adults and Adolescents 12 Years and Older	
Patient Body Weight (kg)	Recommended Oral Dose
Less than 80 kg	One 40mg tablet (blister card contains one 40mg tablet) 40 mg/20 mL (1 bottle) taken as a single dose
At least 80 kg	One 80mg tablet (blister card contains one 80mg tablet) 80mg/40 mL (2 bottles) taken as a single dose

Per the prescribing information, Xofluza is available as 1 x 40mg tablet per blister card and 1 x 80mg tablet per blister card.[3] According to the compendia, Xofluza is also still available as 2 x 20mg tablets per blister card, and 2 x 40mg tablets per blister card.[5] Xofluza is also available as an oral suspension for constitution containing 40mg/20mL (2mg/mL). This dosage form can be used for oral or enteral use. Constituted oral suspension can be stored at room temperature. Xofluza for oral suspension contains no preservative and must be administered within 10 hours after constitution.[3]

Each dose of Xofluza is provided by 1 or 2 tablets (depending on tablet strength), or the maximum of 2 bottles based on body weight. Therefore, the initial limit will be 4 tablets of 20mg (2 tablets per blister card), 4 tablets of 40mg (2 tablets per blister card), 2 tablets of 40mg (1 tablet per blister card), 2 tablets of 80mg (1 tablet per blister card), or 80mL (4 bottles of 40mg/20mL) which allows for 2 doses, accommodating 2 courses of therapy of 1 dose each for treatment or post-exposure prophylaxis, per 90 days.

REFERENCES

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Reviewed:	Medical Affairs 09/1999, 12/1999, 12/2000, 01/2001, 12/2002, 11/2003, 10/2004, 08/2005; (MM) 01/2006, 04/2006; (WF) 02/2007, 07/2007, 03/2008, 03/2009; (KP) 01/2010, 12/2010, 07/2011, 01/2012; (LMS) 12/2012; (LMS) 12/2013; (LCB) 12/2014, (JG) 12/2016, (ME) 12/2017, (SD) 11/2018, (EPA) 12/2018, CHART: 09/2019, (CHART) 12/03/2020, (CHART) 08/26/2021
External Review:	05/2002, 03/2003, 12/2003, 11/2004, 08/2005, 04/2006, 06/2007, 06/2008, 05/2009, 06/2009, 02/2010, 05/2011, 03/2012, 4/2013, 3/2014, 04/2014, 02/2015, 04/2015, 04/2016, 04/2017, 02/2018, 11/2018, 04/2019, 12/2019, 12/2020, 12/2021

LIMIT CRITERIA

Limits should accumulate across all drugs and strengths up to highest quantity listed depending on the order the claims are processed. Accumulation does not apply if limit is coded for daily dose.

Medication	Strength	Limit*
Relenza (zanamivir)	5 mg blister per inhalation	40 blisters / 90 days
Tamiflu (oseltamivir)	6 mg/mL suspension	360 mL / 90 days
	30 mg per capsule	40 capsules / 90 days
	45 mg per capsule	20 capsules / 90 days
	75 mg per capsule	20 capsules / 90 days
Xofluza (baloxavir marboxil)	20 mg per tablet (2 tablets per blister card)	4 tablets / 90 days
	40 mg per tablet (1 tablet per blister card)	2 tablets / 90 days
	40 mg per tablet (2 tablets per blister card)	4 tablets / 90 days
	80 mg per tablet (1 tablet per blister card)	2 tablets / 90 days
	40 mg/20mL suspension	80 mL / 90 days

**These drugs are for short-term acute use; therefore the 3 month limit will be the same as the 1 month limit.*