**Medication Policy Manual**

**Policy No:** dru113  
**Topic:** Relenza®, zanamivir  
**Date of Origin:** December 1, 2004  
**Committee Approval Date:** July 10, 2015  
**Next Review Date:** July 2016  
**Effective Date:** August 1, 2015

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

*Benefit determinations should be based in all cases on the applicable contract language.* To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Zanamivir (Relenza®) is an anti-viral medication (neuraminidase inhibitor) administered via oral inhalation for the treatment or prevention of influenza. It should not be considered a substitute for annual influenza vaccination.

For treatment of influenza, the FDA-approved dose of zanamivir is two inhalations twice daily for five days. [20 inhalations = 5 Rotadisks = 1 course]

For prevention of influenza in a household setting, the FDA-approved dose of zanamivir is two inhalations once daily for ten days. [20 inhalations = 5 Rotadisks = 1 course]
Policy/Criteria

I. Most contracts require prior authorization approval of zanamivir prior to coverage of quantities greater than 40 inhalations (two courses) every six months for the treatment of influenza. Zanamivir in quantities up to 40 inhalations every six months may be considered medically necessary and may be covered without authorization.

II. Zanamivir in quantities up to 60 inhalations (a 30-day course) every six months may be considered medically necessary for seasonal prophylaxis of influenza when both criteria A and B below are met.
   A. The current influenza vaccination is contraindicated or not effective against prevalent circulating strains.
   AND
   B. There is a high risk of complications from influenza (see Appendix 1 for high risk criteria).

III. Administration, Quantity Limitations and Authorization Period
   A. OmedaRx considers zanamivir to be a self-administered medication.
   B. When policy criteria are met, zanamivir may be authorized in quantities of 60 inhalations (a 30-day preventative course) every six months. Quantities exceeding 60 inhalations every six months are considered investigational.
   C. Authorization shall be reviewed every six months to confirm that medical necessity criteria are met.

Position Summary
- Influenza vaccination is the primary method for preventing influenza and its severe complications particularly in individuals at high risk for influenza-related complications. [18]
- Zanamivir, a neuraminidase inhibitor that is given via oral inhalation, has activity against the influenza A and B virus. It has only been shown to be effective for the treatment of influenza if started within the first two days (48 hours) of symptom onset. [2-8]
- The demonstrated benefit with neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir) is limited to a modest improvement in symptoms.
- One treatment course of zanamivir every six months will provide coverage for the typical influenza season.
- The safety and effectiveness of concomitant administration of oseltamivir and zanamivir, or zanamivir and peramivir have not been established. [22]
Background

- There is renewed interest in use of zanamivir because of the high rates of resistance reported to amantadine and rimantadine (up to 92% of influenza A and B isolates). [18]
- Oseltamivir- and zanamivir-resistant strains of influenza A have also begun to emerge as use of the newer antiviral medications increases.
  * Because the rates of resistance are relatively low, oseltamivir and zanamivir are still recommended by the CDC as preferred options for chemoprophylaxis in high-risk individuals after exposure to influenza. [18]
  * Immunization with influenza vaccine as a means to prevent influenza may help limit unnecessary exposure to oseltamivir and zanamivir, thereby slowing the spread of resistance to these medications.
- According to the CDC, influenza vaccination is the primary method for preventing influenza and its severe complications particularly in individuals at high risk for influenza-related complications. [17, 18] High-risk patients are defined in Appendix 1.
- Zanamivir does not have activity against bacterial infections. [9] The FDA has received reports of patients with serious bacterial infections who initially had influenza-like symptoms and who had progressions of bacterial infection during treatment with antiviral drugs alone. [8]

Clinical Efficacy

Treatment of acute influenza:

- Treatment of influenza A or B with zanamivir, oseltamivir, or peramivir decreases the duration of symptoms by about a day in both adult and pediatric patients when compared to placebo. [2-8, 14, 20-21, 23]
- A Cochrane review noted that the quality of the data for neuraminidase inhibitors is extremely poor due to missing study details and the high likelihood of publication and reporting bias. They state that it is not possible to draw robust and unequivocal conclusions with regard to the efficacy of these products. [20]
- Treatment with zanamivir provided no benefit in the time it took patients with influenza to return to normal activity levels. [20]
- The potential benefit versus risk with zanamivir has not been established in patients at high risk for complication from influenza.
  * Safety and efficacy of zanamivir has not been established in subjects with respiratory diseases including but not limited to asthma and chronic obstructive pulmonary diseases. [1]
  * Studies assessing zanamivir in patients with mild to severe asthma showed no improvement in primary respiratory endpoint measures. However, these studies were not sufficiently powered to show differences between zanamivir and placebo. [16, 17]
- Concomitant administration of oseltamivir plus zanamivir has not been shown improve clinical outcomes such as resolution of influenza symptoms when compared with oseltamivir alone. [22]
Prevention of influenza (community outbreak):
- There are randomized clinical trials that show zanamivir was effective in reducing the spread of influenza among household members of the infected patients. [10, 11]
- Zanamivir has been studied in nursing home patients for community outbreak prophylaxis. [12] The efficacy of zanamivir in preventing influenza could not be conclusively established due to the small sample size (n=23). [12]
- There are no trials that directly compare the efficacy or effectiveness of oseltamivir (Tamiflu), zanamivir (Relenza), or peramivir (Rapivab) with influenza vaccine in the prevention of influenza.

Avian influenza (‘bird flu’) and H1N1 influenza (‘swine flu’):
- There is no reliable evidence for neuraminidase inhibitors (oseltamivir, zanamivir, and peramivir) with regard to their efficacy in the treatment or prevention of avian influenza (‘bird flu’) or H1N1 influenza (‘swine flu’). The potential for efficacy in these populations is based on in vitro virological data and extrapolation from use in treating ordinary human influenza.

Dosing and administration
- Zanamivir is administered by oral inhalation, using a Diskhaler device. [1]
- Dosing of zanamivir:
  * Treatment of influenza in adults and children 7 years of age and older: two inhalations (one, 5-mg blister per inhalation for a total dose of 10 mg) twice daily for five days. [1]
  * Prophylaxis of influenza in adults and children 5 years of age and older in the household setting: two inhalations (one 5 mg blister per inhalation for a total dose of 10 mg) once daily for ten days. [1]
  * Prophylaxis of influenza during community outbreaks in adults and adolescents: two inhalations (one 5 mg blister per inhalation for a total dose of 10 mg) once daily for 28 days. [1]
- Most elderly patients are unable to self-administer zanamivir. Improper administration decreases the effectiveness of zanamivir. [13]
- Zanamivir can be administered with inactivated trivalent influenza vaccine without affecting the vaccine induced immune protection. [1, 15]

How supplied
- Zanamivir (Relenza) is supplied in a ROTODISK (circular, double-foil packets) containing four blisters of the drug (a one-day supply per circular packet). Each zanamivir (Relenza) kit contains a DISKHALER device plus five ROTODISKS (enough for one treatment course of medication).
Safety

- Zanamivir is well tolerated with an incidence of side effects similar to that of the vehicle (lactose) alone. \[^1\]

Preventing the spread of influenza: \[^21\]

- Influenza is thought to spread mainly by person-to-person through coughing or sneezing of infected people.
  - Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it.
  - Wash your hands often with soap and water, especially after you cough or sneeze. Alcohol-based hand cleaners are also effective.
  - Avoid touching your eyes, nose, or mouth. Germs spread that way.
  - Stay home if you get sick. The CDC recommends that you stay home from work or school and limit contact with others to keep from infecting them.
Appendix 1: Individuals at High Risk for Complications from Influenza. [18]

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<tr>
<td>1</td>
<td>Equal to or greater than 50 years old.</td>
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<td>2</td>
<td>All children aged 6–59 months.</td>
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<td>3</td>
<td>Residents of nursing homes and other chronic-care facilities with residents of any age who have chronic medical conditions.</td>
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<td>Adults and children with underlying chronic medical conditions such as</td>
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<td>a. Chronic pulmonary diseases (e.g., asthma or chronic airway obstructive disorders)</td>
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<td>b. Cardiovascular disease (except isolated hypertension)</td>
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<td>c. Endocrine (e.g. diabetes) and chronic metabolic disorders</td>
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<td>d. Kidney dysfunction and liver disorders</td>
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<td>e. Blood disorders (e.g., hemoglobinopathies)</td>
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<td>f. Immune system problems (e.g., HIV infection; immunosuppressed by medication, chemotherapy, or radiation therapy)</td>
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<td>g. Neurological or neuromuscular disorders (such as spinal cord injuries, neuromuscular disorders, cognitive dysfunction)</td>
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<td>h. Morbid obesity (BMI of 40 or greater)</td>
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<td>5</td>
<td>Children and adolescents aged 6 months to 18 years on chronic aspirin therapy. These patients may be at risk for developing Reye's syndrome after influenza infection.</td>
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<td>All women who will be pregnant during the influenza season.</td>
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<td>American Indians and Alaskan Natives</td>
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Cross References

Tamiflu®, oseltamivir, Medication Policy Manual, Policy No. 38
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References


21. U.S. Centers for Disease Control and Prevention. Interim guidance on antiviral recommendations for patients with confirmed or suspected Swine Influenza A (H1N1) virus infection in close contacts. Available at: [http://www.cdc.gov/h1n1flu/recommendations.htm#table1](http://www.cdc.gov/h1n1flu/recommendations.htm#table1). Accessed on May 1, 2009.


23. Center for Drug Evaluation and Research. Approval package for Rapivab (peramivir), application number NDA 206426; Medical Review. 12/23/2013. [cited June 10, 2015]; Available from: [http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/206426Orig1s000TOC.cfm](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/206426Orig1s000TOC.cfm)