

**March 2006**

## **Flu Drugs**

### **What drugs are available?**

Four drugs are available to treat and/or prevent influenza. They are amantadine and rimantadine, zanamivir, and oseltamivir.

Because of influenza A virus resistance to rimantadine and amantadine, CDC recommends against using these drugs to prevent and treat flu during the 2005-2006 flu season.

### **How do they work?**

In 1976, the Food and Drug Administration (FDA) approved amantadine to both treat and prevent influenza type A in adults and children 1 year old or older. FDA approved rimantadine—a derivative of amantadine—in 1993 to treat and prevent influenza infection in adults and prevent influenza in children.

These two drugs act against influenza A viruses but not against influenza B viruses. These compounds inhibit the activity of the influenza virus M2 protein, which forms a channel in the virus membrane. As a result, the virus cannot replicate (make copies of itself) after it enters a cell. The drug manufacturers recommend daily doses for using amantadine and rimantadine to treat and prevent the flu in different age groups. Researchers, however, have not adequately evaluated amantadine and rimantadine in children younger than 1 year old.

In 1999, FDA approved two additional drugs to fight the flu: Relenza (zanamivir) and Tamiflu (oseltamivir), the first of a new class of antiviral drugs called neuraminidase inhibitors.

The surfaces of influenza viruses are dotted with neuraminidase proteins. Neuraminidase, an enzyme, breaks the bonds that hold new virus particles to the outside of an infected cell. Once the enzyme breaks these bonds, this sets free new viruses that can infect other cells and spread infection. Neuraminidase inhibitors block the enzyme's activity and prevent new virus particles from being released, thereby limiting the spread of infection.

### **Are these drugs effective against any kind of influenza virus?**

Rimantadine and amantadine are effective only against type A influenza. Zanamivir and oseltamivir inhibit both influenza A and B viruses.

### **Who should consider using these drugs?**

Amantadine is approved for treating and preventing uncomplicated influenza A virus infection in adults and children who are 1 year of age or older. Rimantadine is approved for treating and preventing uncomplicated influenza virus A infection in adults and for preventing, but not treating, such infections in children.

Zanamivir is approved for preventing influenza A and B virus infections in people 5 years of age and older and for treating uncomplicated influenza virus infection in people 7 years of age and older who have not had symptoms for more than 2 days.

Oseltamivir is approved for treating uncomplicated influenza virus infection in people 1 year of age or older who have not had symptoms for more than 2 days. A pediatric liquid formulation is available for oseltamivir. Oseltamivir also is approved for preventing influenza A and B in people 1 year of age and older. Currently, oseltamivir is the only neuraminidase inhibitor approved to prevent the flu.<sup>1</sup>

### **How are these drugs administered?**

Amantadine and rimantadine are taken orally in pill form.

Zanamivir, available as a dry powder, can be inhaled using a device known as a "Diskhaler." The recommended dosage is two inhalations twice a day, morning and night, for 5 days.

Oseltamivir is available as a pill and for adults is taken twice daily for 5 days. For children, the dose of oseltamivir depends on the child's weight. A liquid suspension of oseltamivir can be taken by children or adults who cannot swallow a capsule.

### **How much do these drugs help?**

Studies have shown that all four drugs can reduce the duration of flu symptoms by 1 day if taken within 2 days of the onset of the illness. There is no information about how effective these drugs are if treatment is started more than 2 days after onset of flu symptoms.

When taken as directed to prevent the flu, oseltamivir can significantly reduce your chance of getting the disease if there is a flu outbreak in your family or community. Amantadine and rimantadine have been reported to prevent the spread of influenza A outbreaks primarily in nursing homes. If someone in your family is diagnosed with influenza, taking one of these drugs may reduce the chances of getting the disease.

### **What other benefits might they have?**

None of the four drugs has been shown to effectively prevent serious influenza-related complications such as bacterial or viral pneumonia. Studies of the use of zanamivir in families and in nursing homes at risk for influenza infection, however, resulted in the reduced use of antibiotics, which are frequently prescribed to treat these serious complications.

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<sup>1</sup> **Note to readers:** This information is no longer current. FDA recently approved Zanamivir for as well.

**What about side effects?**

The neuraminidase inhibitors generally cause fewer side effects than the older flu drugs. The most common side effects seen with oseltamivir are nausea and vomiting. In some people, zanamivir can cause wheezing or serious breathing problems that need prompt treatment. The other most common side effects seen with zanamivir include headache and diarrhea. Amantadine and rimantadine can cause side effects such as insomnia and anxiety, nausea or loss of appetite. In some cases, severe side effects such as seizures have been reported.

Your health care provider or pharmacist can discuss with you a more complete list of possible side effects.

**Should certain people not take these drugs?**

People allergic to these drugs or their ingredients should not take them.

Zanamivir generally is not recommended for people with chronic respiratory diseases such as asthma or chronic obstructive pulmonary disease (COPD). In clinical studies, some patients with mild or moderate asthma or COPD had bronchospasm (wheezing) after taking zanamivir. If you have an underlying respiratory disease and have been prescribed zanamivir, your health care provider should instruct you to have a fast-acting inhaled bronchodilator available for use when taking the drug.

The dosage of oseltamivir may need to be adjusted if you have any type of kidney disease.

None of these drugs is recommended for routine use during pregnancy or nursing. These drugs have not been evaluated in pregnant women, and researchers do not know the effects these drugs could have on the unborn child.

In laboratory and in limited clinical studies, there have been no reported interactions of the neuraminidase inhibitors with other drugs.

For complete safety information about these drugs, talk with your pharmacist or health care provider.

**Can influenza viruses develop resistance to these drugs?**

When either amantadine or rimantadine is used for therapy, drug-resistant flu viruses may appear in about one-third of patients.

Laboratory studies have shown that influenza A and B viruses can develop resistance to zanamivir and oseltamivir. Surveillance for neuraminidase inhibitor-resistance has been started.

Because of influenza A virus resistance to rimantadine and amantadine, CDC recommends against using these drugs to treat flu during the 2005-2006 flu season.

## How do the flu drugs compare?

No study to date has directly compared the effectiveness of zanamivir, oseltamivir, amantadine, and rimantadine for treating influenza A or zanamivir and oseltamivir for treating influenza A or B. The available information suggests that these four drugs are similarly effective in reducing the duration of uncomplicated acute illness due to influenza A.

Zanamivir and oseltamivir differ from amantadine and rimantadine in terms of their side effects and cost. Use of amantadine, and to a lesser extent rimantadine, has been associated with central nervous system side effects including nervousness, anxiety, insomnia, and lightheadedness. These side effects have not been associated with zanamivir or oseltamivir. On the other hand, zanamivir and oseltamivir are significantly more expensive than either rimantadine or amantadine. All four drugs are available by prescription only, and it is best to consult with your health care provider to determine what drug might be best for you.

Prepared by:  
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*Last Updated March 31, 2006 (alt)*

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