

Zanamivir

8:18.28 Neuraminidase Inhibitors (AHFS primary); am800 (VA primary)

■ Zanamivir, a sialic acid derivative, is a neuraminidase inhibitor antiviral agent that is pharmacologically related to oseltamivir and active against influenza A and B viruses.

Uses

■ Treatment of Seasonal Influenza A and B Virus Infections

Zanamivir is used for the symptomatic *treatment* of uncomplicated acute illness caused by susceptible influenza A or B virus in adults, adolescents, and children 7 years of age or older who have been symptomatic for no longer than 2 days.

Efficacy of zanamivir for the treatment of influenza is *not* established in patients with underlying airways disease (e.g., asthma, chronic obstructive pulmonary disease [COPD]). In addition, zanamivir is *not* recommended for use in patients with underlying airways disease because of the risk of serious bronchospasm. (See Individuals with Asthma or COPD under Cautions.) Treatment with zanamivir has not been shown to reduce the risk of transmission of influenza to others.

The US Centers for Disease Control and Prevention (CDC), American Academy of Pediatrics (AAP), and Infectious Diseases Society of America (IDSA) recommend treatment of influenza illness in all individuals with suspected or confirmed influenza who require hospitalization (regardless of vaccination status or underlying illness) and in individuals with suspected or confirmed influenza who are at high risk of developing complications (regardless of vaccination status or influenza severity). Early empiric treatment also should be considered for individuals with suspected or confirmed influenza who are at increased risk for influenza-related complications, including children younger than 2 years of age, adults 65 years of age or older, pregnant women and women up to 2 weeks postpartum (including following pregnancy loss), individuals of any age with certain chronic medical or immunosuppressive conditions, individuals younger than 19 years of age who are receiving long-term aspirin therapy, and residents of any age in nursing homes or other long-term care facilities. If treatment is indicated, it should be initiated as early as possible since benefit is greatest if started within 48 hours of symptom onset; initiation of treatment should not be delayed while waiting for laboratory confirmation.

Viral surveillance data available from local and state health departments and the CDC should be considered when selecting an antiviral for treatment of seasonal influenza. Strains of circulating influenza viruses and the antiviral susceptibility of these strains constantly evolve, and the possibility that emergence of zanamivir-resistant influenza virus may decrease effectiveness of the drug should be considered. When treatment of seasonal influenza is indicated, oseltamivir or zanamivir usually is recommended. If viral surveillance indicates that influenza strains resistant to oseltamivir are circulating and treatment is indicated, zanamivir should be used.

CDC issues recommendations concerning the use of antiviral agents for the treatment of influenza, and these recommendations are updated as needed during each influenza season. Information regarding influenza surveillance and updated recommendations for treatment of seasonal influenza are available from CDC at <http://www.cdc.gov/flu>.

Clinical Experience

Efficacy of zanamivir for the treatment of influenza has been established in randomized placebo-controlled studies in which the predominant influenza infection was *seasonal* influenza A; a smaller number of patients in these studies were infected with *seasonal* influenza B. When used within 2 days of onset of symptoms in otherwise healthy adults, adolescents, and children with uncomplicated influenza, the drug has decreased viral shedding in adults and adolescents and reduced the degree and duration of fever, headache, myalgia, cough, and sore throat in adults, adolescents, and children. Zanamivir therapy generally has been associated with a median 1- to 1.5-day decrease in the duration of symptoms, although those who initiate therapy sooner (i.e., no later than 30 hours after symptom onset) and those with more pronounced illness may exhibit greater benefit (e.g., a 3-day decrease in symptom duration).

The comparative efficacy of oseltamivir versus zanamivir in the treatment of influenza A or B virus infections caused by susceptible strains have not been evaluated.

■ Prevention of Seasonal Influenza A and B Virus Infections

Zanamivir is used for the *prophylaxis* of influenza virus infection in adults, adolescents, and children 5 years of age and older.

Safety and efficacy of zanamivir have been established for prophylaxis of seasonal influenza in household settings and during community outbreaks; efficacy of the drug has *not* been established for prophylaxis of seasonal influenza in nursing home settings.

Annual vaccination with seasonal influenza virus vaccine, as recommended by the US Public Health Service Advisory Committee on Immunization Practices (ACIP), is the primary means of preventing seasonal influenza and its severe complications. Prophylaxis with an appropriate antiviral agent active against circulating influenza strains is considered an adjunct to vaccination for the control and prevention of influenza.

When seasonal influenza viruses are circulating in the community, postexposure prophylaxis with oseltamivir or zanamivir can be considered for certain individuals, including those at high risk of developing influenza complications for whom influenza vaccine is contraindicated, unavailable, or expected to have low efficacy (e.g., immunocompromised individuals). Other possible candidates for antiviral prophylaxis include unvaccinated health care personnel, public health workers, and first responders with unprotected, close-contact exposure to a patient with confirmed, probable, or suspected influenza during the time when the patient was infectious. Antiviral prophylaxis also can be considered for controlling influenza outbreaks in nursing and long-term care facilities or other closed or semi-closed settings with large numbers of individuals at high risk for influenza complications. In individuals at high risk of influenza complications who receive influenza virus vaccine inactivated, use of prophylaxis can be considered during the 2 weeks after vaccination to provide protection until an adequate immune response develops. (See Drug Interactions: Influenza Virus Vaccines.)

Viral surveillance data available from local and state health departments and the CDC should be considered when selecting an antiviral for the prophylaxis of influenza. The most appropriate antiviral for prevention of influenza is selected based on information regarding the likelihood that the influenza strain is susceptible and the known adverse effects of the drug. Strains of circulating influenza viruses and the antiviral susceptibility of these strains constantly evolve, and the possibility that emergence of zanamivir-resistant influenza virus may decrease effectiveness of the drug should be considered.

CDC issues recommendations concerning the use of antiviral agents for prophylaxis of influenza, and these recommendations are updated as needed during each influenza season. Information regarding influenza surveillance and updated recommendations for prevention of seasonal influenza are available from CDC at <http://www.cdc.gov/flu>.

Clinical Experience

Efficacy of zanamivir for prevention of *seasonal* influenza was demonstrated in postexposure prophylaxis studies in households and seasonal prophylaxis studies during community outbreaks of influenza. The primary efficacy endpoint in these studies was the incidence of symptomatic, laboratory-confirmed influenza, which was defined as the presence of at least 2 symptoms (oral temperature 37.8°C or higher, feverishness, cough, headache, sore throat, myalgia) and laboratory confirmation by culture, polymerase chain reaction (PCR), or seroconversion.

In the placebo-controlled studies evaluating zanamivir for postexposure prophylaxis in household contacts of an index case, each household (including all household members 5 years of age or older) was randomized to receive zanamivir (10 mg once daily for 10 days) or placebo initiated within 1.5 days of symptom onset in the index cases. The proportion of households with at least 1 new case of symptomatic, laboratory-confirmed influenza was 4.1% in the groups that received zanamivir and 19% in the groups that received placebo.

In a placebo-controlled seasonal prophylaxis study in university students (86% were unvaccinated), the incidence of symptomatic, laboratory-confirmed influenza was 2% in those who received zanamivir (10 mg once daily for 28 days) and 6.1% in those who received placebo during a community outbreak. In another seasonal prophylaxis study in adults and children 12–94 years of age (33% were unvaccinated), the incidence of symptomatic, laboratory-confirmed influenza was 0.2% in those who received zanamivir and 1.4% in those who received placebo during a community outbreak.

■ Avian Influenza A Virus Infections

No clinical data are available to date regarding the use of zanamivir for the treatment of avian influenza A virus infections. Oseltamivir is considered the drug of choice for the treatment of strongly suspected or clinically confirmed cases of avian influenza A (H5N1) infection.

Zanamivir has been suggested as an alternative to oseltamivir for prophylaxis of avian influenza A infections when chemoprophylaxis is indicated in certain exposure situations. (See Prevention under Avian Influenza A Virus Infections: Treatment and Prevention, in Uses in Oseltamivir 8:18.28.)

For information on avian influenza A virus infections, including current recommendations for treatment and prevention, see Uses: Avian Influenza A Virus Infections in Oseltamivir 8:18.28.

■ Pandemic Influenza

Zanamivir is used for the treatment or prevention of pandemic influenza† caused by susceptible strains of influenza virus.

Influenza viruses can cause seasonal epidemics and, occasionally, pandemics during which rates of illness and death from influenza-related complications can increase dramatically worldwide. The most recent influenza pandemic occurred during 2009 and was related to a novel influenza A (H1N1) strain.

On June 11, 2009, the World Health Organization (WHO) declared that the first global influenza pandemic in 41 years was occurring and issued a phase 6 pandemic alert regarding 2009 influenza A (H1N1). A phase 6 pandemic is characterized by human-to-human spread of an animal or human-animal reassortant virus and sustained community level outbreaks of the virus in at least 2 countries in a single WHO region and sustained community level outbreaks in at least one other country in a different WHO region. Cases of human infection with 2009 influenza A (H1N1) were first

reported in Mexico and other countries (including the US) beginning in March and April 2009. The 2009 pandemic influenza A (H1N1) virus is a triple-reassortant swine influenza virus with genes from human, swine, and avian influenza A viruses, and contains a unique combination of gene segments not previously reported in the US or elsewhere. In the US, the 2009 influenza A (H1N1) pandemic was characterized by a substantial increase in influenza activity that peaked in late October and early November 2009 and returned to seasonal baseline levels by January 2010. During that time, more than 99% of influenza viruses circulating in the US were the 2009 pandemic influenza A (H1N1) virus. As of August 2010, the WHO declared that the world was in a post-pandemic period; however, the 2009 influenza A (H1N1) virus is expected to continue to circulate during the 2010–2011 influenza season.

The spread of the highly pathogenic H5N1 strain of avian influenza A in poultry in Asia and other countries that was identified in 2003 represents a potential future pandemic threat. (See Uses: Avian Influenza A Virus Infections, in Oseltamivir 8:18.28.)

Dosage and Administration

Administration

Zanamivir powder for inhalation is administered *only* by oral inhalation using the inhaler (Diskhaler[®]) provided by the manufacturer. The powder for inhalation should *not* be administered using a nebulizer or mechanical ventilator.

Zanamivir has been administered IV†, but a parenteral dosage form of the drug is not commercially available in the US.

Oral Inhalation

Zanamivir powder for inhalation is commercially available in a disk containing 4 foil blisters of the drug (Rotadisk[®]) and is provided with an inhaler (Diskhaler[®]) that is used to deliver the drug to the respiratory tract.

The commercially available powder for inhalation should *not* be removed from its foil blister packaging. The powder should *not* be dissolved or reconstituted in any liquid and should *not* be administered using a nebulizer or mechanical ventilator. (See Administration Precautions under Warnings/Precautions: General Precautions, in Cautions.)

The manufacturer's instructions should be consulted for information on how to load the Rotadisk[®] onto the drug delivery system (Diskhaler[®]) and how to use the Diskhaler[®] to administer the drug.

Patients should be instructed in the safe and effective use of the Diskhaler[®], and instructions should include a demonstration whenever possible.

Patients scheduled to use an inhaled bronchodilator at the same time as zanamivir should use the bronchodilator before zanamivir.

Dosage

Treatment of Seasonal Influenza A and B Virus Infections

For the *treatment* of influenza infection in adults, adolescents, and children 7 years of age or older, the usual dosage of zanamivir is 2 inhalations (one 5-mg blister per inhalation for a total dose of 10 mg) twice daily (about 12 hours apart) for 5 days. Two doses should be administered the first day provided there is an interval of at least 2 hours between doses. On subsequent days, zanamivir doses should be administered about 12 hours apart (e.g., morning and evening) at about the same time each day.

Zanamivir therapy should be initiated within 2 days after the onset of symptoms and usually is continued for 5 days. Although efficacy has not been established if treatment begins more than 2 days after onset of symptoms, studies in patients hospitalized with influenza suggest that antiviral treatment initiated more than 48 hours after onset of symptoms may still be beneficial in patients with moderate to severe or progressive influenza. In addition, patients hospitalized with severe infections (e.g., those with prolonged infection or admitted into an intensive care unit) may require more than 5 days of antiviral treatment.

Prevention of Seasonal Influenza A and B Virus Infections

Household Setting.

For the *prophylaxis* of influenza in adults, adolescents, and children 5 years of age or older in household settings, the usual dosage of zanamivir is 2 inhalations (one 5-mg blister per inhalation for a total dose of 10 mg) once daily for 10 days. The daily dose should be administered at approximately the same time each day.

Efficacy of zanamivir for prophylaxis in household settings is not established if the drug is initiated more than 1.5 days after the onset of symptoms in the index case.

Community Outbreak.

For the *prophylaxis* of influenza in adults and adolescents in community settings, the usual dosage of zanamivir is 2 inhalations (one 5-mg blister per inhalation for a total dose of 10 mg) once daily for 28 days. The daily dose should be administered at approximately the same time each day.

Efficacy of zanamivir for prophylaxis in community outbreaks is not established if the drug is initiated more than 5 days after the outbreak is identified in the community. The safety and efficacy of zanamivir prophylaxis given for longer than 28 days have not been evaluated.

Special Populations

Dosage adjustment is not needed in patients with renal impairment.

Cautions

Contraindications

History of a hypersensitivity reaction to zanamivir or any ingredient in the formulation (e.g., lactose).

Warnings/Precautions

Respiratory Effects

Serious bronchospasm, including fatalities, have been reported in patients receiving zanamivir; some (but not all) of these patients had chronic underlying pulmonary disease (e.g., asthma, chronic obstructive pulmonary disease [COPD]). (See Individuals with Asthma or COPD under Cautions.) Many of these cases were reported during postmarketing surveillance and causality to the drug is difficult to assess.

Some patients without prior respiratory disease also may have respiratory abnormalities from acute respiratory infection that could resemble adverse drug reactions or increase vulnerability to adverse drug reactions.

Discontinue zanamivir in any patient who experiences bronchospasm or decline in respiratory function; immediate treatment and hospitalization may be required.

Individuals with Asthma or COPD

Zanamivir is not recommended for the treatment or prophylaxis of influenza in individuals with underlying airways disease (e.g., asthma, COPD) because of the risk of serious bronchospasm. (See Respiratory Effects under Cautions.)

Bronchospasm has occurred when zanamivir was used in patients with mild or moderate asthma (but without acute influenza-like illness). When used in patients with acute influenza-like illness superimposed on underlying asthma or COPD, a greater than 20% decline in the forced expiratory volume in 1 second (FEV₁) occurred in more patients receiving the drug than in those receiving placebo.

The benefits and risks should be considered carefully if use of zanamivir is considered for a patient with underlying respiratory disease. If a decision is made to use the drug in such patients, monitor respiratory function carefully and have appropriate supportive care available, including short-acting β -adrenergic bronchodilators.

Sensitivity Reactions

Hypersensitivity Reactions.

Bronchospasm and allergic-like reactions (e.g., oropharyngeal edema, serious skin rash) reported.

If an allergic reaction occurs or is suspected, zanamivir should be discontinued immediately and appropriate treatment initiated.

Neuropsychiatric Events

There have been postmarketing reports of delirium and abnormal behavior leading to self-injury, principally involving children in Japan. The contribution of zanamivir to these events has not been established.

Influenza itself can be associated with a variety of neurologic and behavioral symptoms (e.g., seizures, hallucinations, delirium, abnormal behavior) and fatalities can occur. Although such events may occur in the setting of encephalitis or encephalopathy, they can occur without obvious severe disease.

Patients should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms develop, the risks and benefits of continued therapy with zanamivir should be evaluated.

Concomitant Illness

Safety and efficacy for treatment or prophylaxis of influenza have not been established in patients with high-risk underlying medical conditions. (see Individuals with Asthma or COPD under Cautions)

No data are available regarding use of zanamivir in patients with severe or unstable medical conditions that may require inpatient care.

Differential Diagnosis

When making treatment decisions in patients with suspected influenza, consider the possibility of primary or concomitant bacterial infection for which zanamivir would be ineffective.

Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications of influenza. There is no evidence that zanamivir prevents such complications.

There is no evidence of efficacy in illness caused by any organisms other than influenza A or B.

Administration Precautions

Administer zanamivir powder for inhalation using *only* the inhaler (Diskhaler[®]) provided by the manufacturer. Do *not* remove the powder from its foil blister packaging (Rotadisk[®]). Do *not* attempt to reconstitute or solubilize the powder in liquid; do *not* attempt to administer the drug in a nebulizer or mechanical ventilator.

Safety and efficacy have not been established for administration by nebulization. Lactose in the formulation may obstruct or interfere with proper functioning of mechanical ventilator equipment. At least 1 death has been reported when a patient received the drug by mechanical ventilation after solubilization in a liquid.

Patients should be instructed in the safe and effective use of the drug delivery system (Diskhaler[®]) provided by the manufacturer. Instructions on use of the inhaler should include a demonstration whenever possible.

Some geriatric patients may need assistance with the inhaler.

Children should be under adult supervision with close attention to use of the inhaler. (See Cautions: Pediatric Use.)

Prior Use

No data are available regarding safety and efficacy of repeated courses of zanamivir for treatment of influenza.

Influenza Vaccination

Zanamivir is not a substitute for annual vaccination with seasonal influenza virus vaccine inactivated or seasonal influenza virus vaccine live intranasal.

Although antiviral agents used for treatment or prevention of influenza (amantadine, oseltamivir, rimantadine, zanamivir) may be used concomitantly with seasonal influenza virus vaccine inactivated, seasonal influenza virus vaccine live intranasal should not be administered until at least 48 hours after influenza antiviral agents are discontinued, and these antiviral agents should not be administered until at least 2 weeks after administration of intranasal live influenza virus vaccine. (See Influenza Virus Vaccines under Drug Interactions.)

Specific Populations

Pregnancy.

Category C. (See Users Guide.)

Pregnant women are at increased risk for severe complications and death from influenza. The US Centers for Disease Control and Prevention (CDC) states that pregnancy should not be considered a contraindication to use of zanamivir for the treatment or prevention of influenza and that zanamivir regimens recommended for such infections in pregnant women are the same as those for other adults.

Because of its systemic absorption, CDC states that oseltamivir may be preferred when a neuraminidase inhibitor is indicated for the treatment of influenza in a pregnant woman, but the drug of choice for prophylaxis of these infections is less clear. Zanamivir may be preferred for prophylaxis in pregnant women because of its limited systemic absorption; however, respiratory complications that may be associated with zanamivir because of its route of administration should be considered, especially in women at risk for respiratory problems.

Lactation.

Zanamivir is distributed into milk in rats; caution if used in nursing women.

CDC states that antiviral treatment or prophylaxis is not a contraindication for breastfeeding.

Pediatric Use.

Safety and efficacy for *treatment* of influenza not established in children younger than 7 years of age. Some clinical studies evaluating zanamivir have included children 5–6 years of age[†]; however, there is some evidence that the drug is not as effective in these children as in older children and adults.

Safety and efficacy for *prophylaxis* of influenza not established in children younger than 5 years of age. Safety and efficacy in adolescents and children 5 years of age or older for *prophylaxis* of influenza are similar to adults.

Some young children may have suboptimal inspiratory flow rates through the drug delivery system (Diskhaler[®]). When considering use of zanamivir in pediatric patients, clinicians should carefully evaluate the ability of the child to use the inhaler.

Children should receive zanamivir only under adult supervision and with close attention to proper use of the inhaler. The supervising adult should be instructed on proper use of the inhaler.

Geriatric Use.

Safety and efficacy for *treatment* of influenza in those 65 years of age or older is similar to that reported in younger adults.

Safety and efficacy for *prophylaxis* of influenza in those 65 years of age or older in household or community settings are similar to that reported in younger adults. Efficacy has *not* been established for *prophylaxis* of influenza in geriatric individuals in nursing home settings.

Possibility exists of greater sensitivity to the drug in some older individuals.

Some geriatric patients may need assistance with the drug delivery system

(Diskhaler[®]).

Hepatic Impairment.

Pharmacokinetics not studied in the presence of hepatic impairment.

Renal Impairment.

Safety and efficacy not documented in presence of severe renal impairment, but systemic exposure is limited after oral inhalation. Potential for drug accumulation should be considered.

Common Adverse Effects

Adverse effects occurring in 1–3% or more of adults and children 12 years of age or older include diarrhea; nausea; vomiting; nasal signs and symptoms; bronchitis; sinusitis; cough; ear, nose, and throat infections; headache; and dizziness. No adverse effect occurred at an incidence greater than 3%. Adverse effects occurring in up to 5% of children 5–12 years of age include ear, nose, and throat infections; vomiting; nausea;

and diarrhea. Some adverse effects may be secondary to lactose vehicle inhalation. Bronchospasm and allergic-like reactions, including oropharyngeal edema and serious rash, have been reported.

Drug Interactions

Zanamivir not metabolized by and does not affect cytochrome P-450 (CYP) enzymes, including CYP1A1, 1A2, 2A6, 2C9, 2C18, 2D6, 2E1, or 3A4. Drug interactions with drugs that are substrates or inhibitors of these enzymes unlikely.

Influenza Virus Vaccines

Zanamivir (10 mg daily) does not appear to interfere with the antibody response to influenza virus vaccine inactivated. Inactivated influenza vaccines may be administered concomitantly with zanamivir.

Safety and efficacy of concomitant use of seasonal influenza virus vaccine live intranasal with antiviral agents used for treatment or prevention of influenza (e.g., amantadine, oseltamivir, rimantadine, zanamivir) have not been studied. Because influenza antiviral agents reduce replication of influenza viruses, do not administer seasonal influenza virus vaccine live intranasal until at least 48 hours after zanamivir is discontinued, and do not administer zanamivir until at least 2 weeks after administration of intranasal live influenza vaccine. The US Public Health Service Advisory Committee on Immunization Practices (ACIP) recommends revaccination if an influenza antiviral is given 2 days before to 14 days after vaccination with influenza virus vaccine live intranasal.

Pharmacokinetics

Absorption

Bioavailability

Following oral inhalation of zanamivir, approximately 4–17% of the inhaled dose is absorbed systemically.

Absolute bioavailability averages 2% following oral inhalation; peak serum concentrations attained within 1–2 hours.

Special Populations

In pediatric patients younger than 12 years of age with signs and symptoms of respiratory illness, zanamivir serum concentrations may be low or undetectable following oral inhalation because of inadequate or absent inspiratory flow rates. (See Pediatric Use under Cautions.)

Distribution

Extent

Delivered to epithelial lining of the respiratory tract following oral inhalation. Amount of drug in respiratory tract depends on patient factors such as inspiratory flow rate. May be present in sputum and nasal washings for at least 12 hours after a dose.

Crosses the placenta in animals.

Distributed into milk in animals; not known whether distributed into human milk.

Plasma Protein Binding

Less than 10% bound to plasma proteins.

Elimination

Metabolism

Not metabolized.

Not a substrate for and does not affect CYP isoenzymes.

Elimination Route

Following oral inhalation, absorbed drug is excreted unchanged in urine within 24 hours; unabsorbed drug excreted in feces.

Half-life

Serum half-life following oral inhalation is 2.5–5.1 hours.

Special Populations

Half-life prolonged in those with renal impairment; studies using IV zanamivir indicate half-life is 4.7 hours if mild to moderate impairment and 18.5 hours if severe impairment.

Description

Zanamivir, a sialic acid derivative, is a neuraminidase inhibitor antiviral agent. Zanamivir is pharmacologically related to oseltamivir and, like oseltamivir, is pharmacologically unrelated to other currently available antiviral agents.

Zanamivir is a potent selective competitive inhibitor of the influenza virus neuraminidase, an enzyme essential for viral replication. Neuraminidase cleaves terminal sialic acid residues from glycoconjugates to enable the release of virus from infected cells, prevent the formation of viral aggregates after release from host cells, and possibly decrease viral inactivation by respiratory mucus.

Zanamivir exhibits potent antiviral activity in vitro against both influenza A and B viruses, including amantadine- and rimantadine-resistant isolates. In vitro studies indicate that zanamivir is active against avian influenza A viruses, including influenza A H5N1, H6N1, H7N7, and H9N2. Zanamivir is active against some influenza strains

resistant to oseltamivir. To date, isolates of the 2009 pandemic influenza A (H1N1) virus, including some oseltamivir-resistant strains, have been susceptible to zanamivir.

Resistance to zanamivir has been produced in vitro by serial passage of influenza virus in the presence of increasing concentrations of the drug. The risk of emergence of zanamivir resistance in clinical isolates has not been quantified. Resistant strains of influenza B have emerged in immunocompromised patients receiving the drug. In addition, seasonal influenza A (H1N1) with in vitro resistance to zanamivir have been reported.

Influenza strains cross-resistant to oseltamivir and zanamivir have been generated in cell culture; only limited data are available regarding possible emergence of clinical isolates with cross-resistance to both drugs. Mutations at positions 152 or 292 can confer cross-resistance between oseltamivir and zanamivir. To date, isolates with the H274Y mutation that are resistant to oseltamivir have remained susceptible to zanamivir. Influenza A (H5N1) isolates isolated from a patient in Vietnam during 2005 had mutations associated with oseltamivir resistance but remained susceptible to zanamivir.

Advice to Patients

Importance of understanding proper inhalation technique and use of the drug delivery system (Diskhaler®); importance of reading the patient instructions for use.

Importance of initiating zanamivir treatment as soon as possible after appearance of influenza symptoms (within 2 days after symptom onset); efficacy not established if treatment begins after 48 hours of symptoms.

Advise patients that zanamivir treatment does not reduce the risk of transmission of influenza virus to others.

Advise patients of the possible risk of bronchospasm, especially in those with chronic underlying respiratory disease (e.g., asthma, chronic obstructive pulmonary disease [COPD]); importance of patients with asthma or COPD having a short-acting inhaled β-adrenergic bronchodilator readily available.

Advise patients using an inhaled bronchodilators at the same time as zanamivir of the importance of using the bronchodilator first.

Importance of discontinuing zanamivir and promptly contacting a clinician if there is an increase in respiratory symptoms (e.g., wheezing, dyspnea, signs or symptoms of bronchospasm) or if symptoms of an allergic reaction occur.

Importance of immediately contacting a clinician if patient demonstrates signs of unusual behavior. Influenza patients, particularly children and adolescents, may be at increased risk of seizures, confusion, or abnormal behavior early in their illness and should be closely observed for signs of unusual behavior. Such events are uncommon, but may occur after starting zanamivir treatment or when influenza is not treated and can result in accidental injury to the patient.

Importance of informing clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as any concomitant illnesses.

Importance of women informing clinicians if they are or plan to become pregnant or plan to breast-feed.

Importance of informing patients of other important precautionary information. (See Cautions.)

Overview (see Users Guide). For additional information until a more detailed monograph is developed and published, the manufacturer's labeling should be consulted. It is essential that the manufacturer's labeling be consulted for more detailed information on usual cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.

Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Zanamivir

Oral Inhalation

Powder for inhalation (contained in Rotadisk® foil pack)

5 mg per inhalation

Relenza® (with Diskhaler®),
GlaxoSmithKline

† Use is not currently included in the labeling approved by the US Food and Drug Administration.

Selected Revisions November 2010, © Copyright, September 1999, American Society of Health-System Pharmacists, Inc.