



CLINICAL TOPIC: SWINE INFLUENZA (FLU)

The RxBULLETIN, formerly known as the RxDISPATCH, is intended to provide you with important news bulletins related to drugs and the pharmaceutical industry.

Importance of this Topic

- Human cases of swine influenza A (H1N1) have been reported worldwide.
- Deaths due to swine influenza A (H1N1) infection have occurred. Deaths have been reported in Mexico; to date, no deaths have been reported in the United States (U.S.).
- There is no vaccine against the current virus strain (H1N1) causing these cases of swine influenza. It is not known if current human seasonal influenza vaccines provide any protection against the H1N1 swine influenza A.
- The possibility of swine influenza becoming a pandemic is a concern. A *pandemic flu* is virulent human flu that causes a global outbreak, or pandemic, of serious illness. Because there is little natural immunity, the disease can spread easily from person to person.
- Laboratory testing has found the swine influenza A (H1N1) virus is susceptible to the prescription antiviral drugs oseltamivir (Tamiflu[®]) and zanamivir (Relenza[®]).
- For clients, it should be recognized that Tamiflu and Relenza may be subject to utilization management strategies such as quantity and/or duration limits; informedRx recommends quantity limits for these drugs as a component of our standard utilization management recommendations. These quantity/duration limitations are intended to prevent inappropriate use and stockpiling under normal circumstances. It is important to note that in a pandemic situation and with guidance from organizations such as the CDC and WHO, revisions to the current QL may be necessary, including the recommendation to remove all such restrictions to better protect patients, especially in the absence of any vaccine. Please note that such guidance has not been given from any organization at this time. Please contact your account manager if you would like to discuss this QL strategy further.
- informedRx recommends that clients with utilization management strategies in place for Tamiflu and Relenza review their policies for these agents and educate their customer service representatives and clinical review pharmacists to ensure appropriate availability of these agents to their members.
- The Department of Health and Human Services, Centers for Medicare & Medicaid Services, Center for Drug and Health Plan Choice issued a memo to all Medicare Part D Sponsors and all Medicare Advantage Organizations regarding the April 26, 2009 Public Health Emergency Declarations and the emergency use of certain products from the neuraminidase class of antivirals oseltamivir phosphate and zanamivir. In the memo, sponsors are recommended to actively monitor the directions provided by the Centers for Disease Control and Prevention (CDC) at <http://www.cdc.gov/swineflu/>, as well as the DHHS website at <http://www.dhhs.gov/> in case further information is released. In addition, it is recommend that sponsors share the scripting included in the memo with their customer service representatives (CSRs) to address questions from enrollees. [Click here to view the memo](#)

Overview: Swine Influenza

- Swine influenza, or “swine flu”, is a highly contagious acute respiratory disease of pigs, caused by one of several swine influenza A viruses. Morbidity tends to be high and mortality low (1-4%). The virus is spread among pigs by aerosols, direct and indirect contact, and asymptomatic carrier pigs. Outbreaks in pigs occur year round, with an increased incidence in the fall and winter in temperate zones. Many countries routinely vaccinate swine populations against swine influenza.
- Swine influenza viruses are most commonly of the H1N1 subtype, but other subtypes are also circulating in pigs (e.g., H1N2, H3N1, H3N2). Pigs can also be infected with avian influenza viruses and human seasonal influenza viruses as well as swine influenza viruses. The H3N2 swine virus was thought to have been originally introduced into pigs by humans. Sometimes pigs can be infected with more than one virus type at a time, which can allow the genes from these viruses to mix. This can result in an influenza virus containing genes from a number of sources, called a "reassortant" virus.
- Although swine influenza viruses are normally species specific and only infect pigs, they do sometimes cross the species barrier to cause disease in humans. Most commonly, these cases occur in persons with direct exposure to pigs (e.g. children near pigs at a fair or workers in the swine industry). Human-to-human transmission of swine flu can also occur. This is thought to occur in the same way as seasonal flu occurs in people, which is mainly person-to-person transmission through coughing or sneezing of people infected with the influenza virus. People may become infected by touching something with flu viruses on it and then touching their mouth or nose.

Who is Affected by the Current Outbreak of Swine Influenza

- According to the World Health Organization (WHO), as of April 27, confirmed cases of swine influenza A (H1N1) have been reported in the following countries: Mexico, Canada, United States, and Spain. Reuters reports that cases of swine influenza A have been identified in Israel and New Zealand as well.
- According to the Centers for Disease Control and Prevention (CDC), as of April 28, confirmed cases of swine influenza A (H1N1) have been reported in the following U.S. states: California, Kansas, New York, Ohio, and Texas.
- Cases have been reported in the young and old, as well as ages in between, and have ranged in severity from mild to severe.

What are the Human Symptoms of Swine Influenza

- The symptoms of swine flu in people are expected to be similar to the symptoms of regular human seasonal influenza and include: fever, lethargy, lack of appetite and coughing. Some people with swine flu also have reported runny nose, sore throat, nausea, vomiting and diarrhea.
- The spectrum of symptoms can range from little to no symptoms to severe pneumonia resulting in death.

What Steps Have Been Taken by World Government Agencies

- The WHO Director-General has raised the level of influenza pandemic alert from the current phase 3 to phase 4. Phases 1–3 correlate with preparedness, including capacity development and response planning activities, while Phases 4–6 clearly signal the need for response and mitigation efforts.
 - In Phase 3, an animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks. Limited human-to-human transmission may occur under some circumstances, for example, when there is close contact between an infected person and an unprotected caregiver. However, limited transmission under such restricted circumstances does not indicate that the virus has gained the level of transmissibility among humans necessary to cause a pandemic.
 - Phase 4 is characterized by verified human-to-human transmission of an animal or human-animal influenza reassortant virus able to cause “community-level outbreaks.” The ability to cause sustained disease outbreaks in a community marks a significant upwards shift in the risk for a pandemic. Any country that suspects or has verified such an event should urgently consult with WHO so that the situation can be jointly assessed and a decision made by the affected country if implementation of a rapid pandemic containment operation is warranted. Phase 4 indicates a significant increase in risk of a pandemic but does not necessarily mean that a pandemic is a forgone conclusion.
- The CDC activated its Emergency Operations Center to coordinate the agency's response to this emerging health threat and on April 27, the Secretary of the Department Homeland Security, Janet Napolitano, declared a public health emergency in the United States. This will allow funds to be released to support the public health response. CDC's goals during this public health emergency are to reduce transmission and illness severity, and provide information to assist health care providers, public health officials and the public in addressing the challenges posed by this newly identified influenza virus. To this end, CDC has issued a number of interim guidance documents in the past 24 hours. In addition, CDC's Division of the Strategic National Stockpile (SNS) is releasing one-quarter of its antiviral drugs, personal protective equipment, and respiratory protection devices to help states respond to the outbreak.
- The U.S. Food and Drug Administration, in response to requests from the U.S. Centers for Disease Control and Prevention, has issued Emergency Use Authorizations (EUAs) to make available to public health and medical personnel important diagnostic and therapeutic tools to identify and respond to the swine flu virus under certain circumstances. The agency issued these EUAs for the use of certain Relenza and Tamiflu antiviral products, and for the rRT-PCR Swine Flu Panel diagnostic test.

Preventative Measures to Minimize the Spread of Swine Influenza

- **Vaccination:** currently, there are no vaccines to protect humans against the current swine influenza virus. It is not known whether current human seasonal influenza vaccines can provide any protection. According to a report in *Scrip*, Sanofi Pasteur has indicated it would be able to produce a vaccine against the outbreak of swine influenza A (H1N1) within three months of receiving the strain from the World Health Organization; additionally it was reported that Sanofi's two plants based in the U.S. and France have the capacity to switch immediately to producing pandemic vaccines if the WHO requests it.
- **General preventative measures/good hygiene practices for influenza:**
 - 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 frequently and thoroughly with soap and water, especially after you cough or sneeze. Alcohol-based hands cleaners are also effective.
 - Avoid touching your eyes, nose or mouth. Germs spread that way.
 - Practice good health habits including getting adequate sleep/rest, eating nutritious food, drinking plenty of fluids, and keeping physically active.
 - Try to avoid close contact with sick people (Influenza is thought to spread mainly person-to-person through coughing or sneezing of infected people).
 - If you get sick, it is recommended that you stay home from work or school and limit contact with others to keep from infecting them.
 - It is considered prudent for people who are ill to delay international travel and for people developing symptoms following international travel to seek medical attention.
 - The CDC recommends that facemasks should be considered for use by individuals who enter crowded settings, both to protect their nose and mouth from other people's coughs and to reduce the wearers' likelihood of coughing on others; the time spent in crowded settings should be as short as possible.
 - If caring for sick person(s):
 - Keep the sick person away from others.
 - Cover your mouth and nose when caring for the sick person.
 - Wash your hands with soap and water thoroughly after each contact with the sick person.
 - Try to improve airflow in the area where the sick person is staying.
 - Keep the area where the sick person is staying clean.
 - The CDC recommends that respirators should be considered for use by individuals for whom close contact with an infectious person is unavoidable. This can include selected individuals who must care for a sick person (e.g., family member with a respiratory infection) at home.
- **Travel:** at this time, the CDC recommends that U.S. travelers avoid all nonessential travel to Mexico. Reuters reports that Canada and the European Union have also advised people to avoid non-essential travel to Mexico. Companies have also adopted wider travel restrictions to countries where cases have been confirmed.

Treatment Measures for Swine Influenza

- At this time, the CDC recommends the use of oseltamivir (Tamiflu[®]) or zanamivir (Relenza[®]) for the treatment and/or prevention of infection with swine influenza viruses.
- Empiric antiviral treatment should be considered for confirmed, probable or suspected cases of swine influenza A (H1N1) virus infection. Treatment of hospitalized patients and patients at higher risk for influenza complications should be prioritized. Antiviral treatment with zanamivir or oseltamivir should be initiated as soon as possible after the onset of symptoms. Evidence for benefits from treatment in studies of seasonal influenza is strongest when treatment is started within 48 hours of illness onset.
- Antiviral doses recommended for treatment of swine influenza A (H1N1) virus infection in adults or children 1 year of age or older are the same as those recommended for seasonal influenza. Oseltamivir use for children < 1 year old was recently approved by the U.S. Food and Drug Administration (FDA) under an Emergency Use Authorization (EUA), and dosing for these children is age-based.
- Antiviral chemoprophylaxis (pre-exposure or post-exposure) with either oseltamivir or zanamivir is recommended for the following individuals:
 - Household close contacts who are at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women) of a confirmed, probable or suspected case.
 - School children who are at high-risk for complications of influenza (children with certain chronic medical conditions) who had close contact (face-to-face) with a confirmed, probable, or suspected case.
 - Travelers to Mexico who are at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women).
 - Health care workers or public health workers who were not using appropriate personal protective equipment during close contact with an ill confirmed, probable, or suspect case of swine influenza A (H1N1) virus infection during the case's infectious period.
- Pre-exposure antiviral chemoprophylaxis with either oseltamivir or zanamivir can be considered for the following:
 - Any health care worker who is at high-risk for complications of influenza (e.g., persons with certain chronic medical conditions, persons 65 or older, children younger than 5 years old, and pregnant women) who is working in an area of the healthcare facility that contains patients with confirmed swine influenza A (H1N1) cases, or who is caring for patients with any acute febrile respiratory illness.
 - Non-high risk persons who are travelers to Mexico, first responders, or border workers who are working in areas with confirmed cases of swine influenza A (H1N1) virus infection.
- The current swine influenza A virus H1N1 is resistant to amantadine (Symmetrel[®]) and rimantadine (Flumadine[®]) and therefore, should not be used.

CDC Swine Influenza Antiviral Medication Dosing Recommendations*				
Trade Name (generic name) Manufacturer	Strength(s) & Dosage Forms(s)	Treatment Dosing [†]	Chemoprophylaxis Dosing [‡]	Cost
Tamiflu (oseltamivir) Roche	30 mg, 45 mg, & 75 mg Capsules; 12 mg/mL Powder for Suspension	Adults: 75 mg twice daily Children (≥ 12 months): administer in 2 divided doses as follows based on weight - ≤ 15 kg: 60 mg/day 15-23 kg: 90 mg/day 24-40 kg: 120 mg/day > 40 kg: 150 mg/day Children < 1 year: administer as follows based on age – < 3 months: 12 mg twice daily 3-5 months: 20 mg twice daily 6-11 months: 25 mg twice daily	Adults: 75 mg once daily Children (≥ 12 months): administer once per day as follows based on weight - ≤ 15 kg: 30 mg/day 15-23 kg: 30 mg/day 24-40 kg: 60 mg/day > 40 kg: 75 mg/day Children < 1 year: administer as follows based on age – < 3 months: not recommended 3-5 months: 20 mg once daily 6-11 months: 25 mg once daily	Capsules: \$101.70 [box of 10 capsules] Suspension: \$50.85 [1 bottle of 25 mL]
Relenza (zanamivir) GlaxoSmithKline	5 mg Powder for Inhalation	Adults: two 5 mg inhalations (10 mg) twice daily Children (≥ 7 years): two 5 mg inhalations (10 mg) twice daily	Adults: two 5 mg inhalations (10 mg) once daily Children (≥ 7 years): two 5 mg inhalations (10 mg) once daily	\$67.19 per 1 inhaler [containing 10 doses]

[†]Recommended duration of treatment is five days.
[‡]Duration of antiviral chemoprophylaxis *post-exposure* is 10 days after the last known exposure to an ill confirmed case of swine influenza A (H1N1) virus infection. For *pre-exposure* protection, chemoprophylaxis should be given during the potential exposure period and continued for 10 days after the last known exposure to an ill confirmed case of swine influenza A (H1N1) virus infection.
*Extracted from IDSA Guidelines for Seasonal Influenza; available at: <http://www.journals.uchicago.edu/doi/pdf/10.1086/598513>
[^]Based on AWP as listed in Medispan as of April 28, 2009.

What Not to Do

- Panic. Do not panic and seek medical attention if you feel ill.
- The WHO Director-General has recommended that countries not close borders and not restrict international travel.
- Individuals do not have to stop eating pork or pork products; eating properly handled and cooked pork and pork products is safe.

Where to Go for Additional Information

- World Health Organization (WHO): <http://www.who.int/en/>
- Centers for Disease Control and Prevention (CDC): <http://www.cdc.gov/>
- U.S. Department of Health and Human Services (HHS): <http://www.dhhs.gov/>
- PandemicFlu.gov: <http://www.pandemicflu.gov/>
- Food and Drug Administration (FDA): <http://www.fda.gov/>
- Agency for Healthcare Research and Quality (AHRQ): <http://www.ahrq.gov/prep/swineflu.htm>

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