Influenza Update

ACTIVITY DESCRIPTION
Influenza (commonly referred to as "the flu") is a contagious viral infection of the respiratory tract (e.g., nose, throat, and lungs). Influenza viruses are primarily spread by respiratory transmission—through droplets from coughing or sneezing. The circulation of influenza viruses varies geographically, with transmission occurring between October and May in the Northern Hemisphere of the temperate region (which includes the US). April and September in the Southern Hemisphere of the temperate region, and year-round in tropical/sub-tropical regions. In the US, peak influenza activity often occurs in January and February. The flu can affect people of all ages, most frequently school-aged children, usually causing asymptomatic infection or mild to moderate illness. Severe illness and death occur most often in vulnerable populations (e.g., infants, elderly, and immunocompromised individuals). Each year, influenza affects 5-20% of the US population and causes 3,000-49,000 deaths from influenza-related complications. In the 2016-2017 season, 31 million Americans were infected, 14.5 million sought medical care, and 600,000 individuals were hospitalized due to influenza. Influenza vaccination is an important primary prevention strategy. The Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination for all persons 6 months and older (unless contraindicated) starting in early fall, as soon as the vaccine becomes available. The vaccine is available in a variety of formulations; however, the ACIP makes no preferential recommendation and encourages vaccination with any licensed, age-appropriate vaccine during the 2018-2019 season. Despite the ACIP’s universal recommendation for influenza vaccination, only 47% of the target population in the US (individuals 6 months and older) received the vaccine during the 2016-2017 season. This issue provides key information on influenza vaccines and antiviral medications for the 2018-2019 flu season, including precautions, side effects, and use in special populations.

TARGET AUDIENCE
The target audience for this activity is pharmacists in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:

- Describe the influenza disease course, symptoms, and diagnostic tests. Recognize people at high risk for flu complications.
- Describe the determinants for influenza vaccine efficacy. Discuss the rationale for the suboptimal efficacy of the 2017-2018 vaccines, and recommendations for the use of LAIV vaccine in 2018-2019.
- State the indications, dosing requirements (children and adults), administration routes, side effects, and contraindications for 2018-2019 influenza vaccinations.
- Discuss the use of antiviral drugs for influenza treatment and prevention; be able to apply the current recommendations for their use.

FINANCIAL SUPPORT BY
Pharmaceutical Education Consultants, Inc.
Richard H. Dang, PharmD, APh, BCACP

Assistant Professor of Clinical Pharmacy, University of Southern California (USC) School of Pharmacy

ABOUT THE AUTHOR
Richard H. Dang, PharmD, APh, BCACP is an Assistant Professor of Clinical Pharmacy, Director of Student Outreach for Community Health, and Site Coordinator of the PGY-1 Community-Based Pharmacy Residency Program at the University of Southern California (USC) School of Pharmacy. Dr. Dang coordinates courses in introductory and advanced community pharmacy practice, self-care/nonprescription therapeutics, and travel medicine. He is licensed as an Advanced Practice Pharmacist and is a national trainer for the APhA Pharmacy-Based Immunization Delivery program, the NACDS Community Pharmacy-Based Point-of-Care Testing Certificate program, and the CPhA/NACDS Advanced Practice Pharmacists Certificate Training Program.

FACULTY DISCLOSURE
It is the policy of PharmCon, Inc. to require the disclosure of the existence of any significant financial interest or any other relationship a faculty member or a sponsor has with the manufacturer of any commercial product(s) and/or service(s) discussed in an educational activity. Richard Dang reports no actual or potential conflict of interest in relation to this activity.

Peer review of the material in this CE activity was conducted to assess and resolve potential conflict of interest. Reviewers unanimously found that the activity is fair balanced and lacks commercial bias.

Please Note: PharmCon, Inc. does not view the existence of relationships as an implication of bias or that the value of the material is decreased. The content of the activity was planned to be balanced and objective. Occasionally, faculty may express opinions that represent their own viewpoint. Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not intended as a substitute for the participant’s own research, or for the participant’s own professional judgement or advice for a specific problem or situation. Conclusions drawn by participants should be derived from objective analysis of scientific data presented from this activity and other unrelated sources.

Neither freeCE/PharmCon nor any content provider intends to or should be considered to be rendering medical, pharmaceutical, or other professional advice. While freeCE/PharmCon and its content providers have exercised care in providing information, no guarantee of its accuracy, timeliness or applicability can be or is made. You assume all risks and responsibilities with respect to any decisions or advice made or given as a result of the use of the content of this activity.
**Introduction**

Influenza (commonly referred to as “the flu”) is a contagious viral infection of the respiratory tract (eg, nose, throat, and lungs). Influenza viruses are primarily spread by respiratory transmission – through droplets from coughing or sneezing. The circulation of influenza viruses varies geographically, with transmission occurring between October and May in the Northern Hemisphere of the temperate region (which includes the US), April and September in the Southern Hemisphere of the temperate region, and year-round in tropical/sub-tropical regions. In the US, peak influenza activity often occurs in January and February.

The flu can affect people of all ages, most frequently school-aged children, usually causing asymptomatic infection or mild to moderate illness. Severe illness and death occur most often in vulnerable populations (eg, infants, elderly, and immunocompromised individuals). Each year, influenza affects 5-20% of the US population and causes 3,000-49,000 deaths from influenza-related complications. In the 2016-2017 season, 31 million Americans were infected, 14.5 million sought medical care, and 600,000 individuals were hospitalized due to influenza.

Influenza vaccination is an important primary prevention strategy. The Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination for all persons 6 months and older who have no contraindications starting in early fall, as soon as the vaccine becomes available. The vaccine is available in a variety of formulations; however, the ACIP makes no preferential recommendation and encourages vaccination with any licensed, age-appropriate vaccine during the 2018-2019 season. Despite the ACIP’s universal recommendation for influenza vaccination, only 47% of the target population in the US (individuals 6 months and older) received the vaccine during the 2016-2017 season. This issue provides key information on influenza vaccines and antiviral medications for the 2018-2019 flu season, including precautions, side effects, and use in special populations.

**The Bottom Line**

- Influenza is a viral infection of the respiratory tract spread through coughing or sneezing or contact with contaminated surfaces. Symptoms typically have a sudden onset and include fever, chills, cough, sore throat, nasal congestion, muscle aches, headache, and fatigue.
- Complications from the flu (more severe infections, worsening of existing diseases) are more common among infants or young children, the elderly, immunocompromised persons, and those with chronic diseases.
- Annual influenza vaccination is recommended in early fall for everyone aged 6 months and older who have no contraindications. Efficacy depends on a patient’s age, overall health, and how well the vaccine matches currently circulating strains.
- Available flu vaccines have varying compositions, age indications, precautions, and formulations (eg, high dose, adjuvant, intradermal, intranasal, needle free). High-dose and adjuvanted vaccines provide better protection in elderly people than standard-dose vaccines.
- Side effects of flu vaccines are uncommon, mild, and self-limiting. Allergic reactions to influenza vaccines are rare. Persons with egg allergy of any severity can get vaccinated, followed by a 15-minute observation period. A history of severe egg allergy warrants vaccination in a medical setting.
- Treatment with antiviral medications should be considered in a patient who is at high risk for complications, has severe or progressive disease, or is hospitalized. Initiate as soon as possible if flu is suspected (with or without diagnostic testing). Preventive use can be considered in similar individuals who have had recent contact with someone with the flu.
Background
There are 3 types of influenza virus that infect people, with types A and B being the most common. Type C is uncommon and typically produces mild disease. Type A viruses account for the majority of cases in most seasons, and have been responsible for influenza pandemics; however, influenza B viruses can also be a public health threat, particularly among children and people who are at greater risk for complications. Influenza A viruses are classified into subtypes based on their surface antigens: hemagglutinin (H) and neuraminidase (N). The glycoproteins of these surface antigens continuously undergo minor mutations (antigenic drift, which may result in epidemics) and major mutations (antigenic shift, which may result in pandemics). These mutations reduce the immune system’s ability to mount an effective response to the virus, since immunity has not been established by prior exposure. Influenza B viruses are not categorized by subtypes, but rather by genetically distinct lineages (either Yamagata or Victoria). In addition to transmission through airborne respiratory secretions, influenza can be spread by touching contaminated surfaces and then touching one’s nose or mouth. The incubation period (the time between exposure and symptom onset) ranges from 1-4 days, with an average of 2 days. Once infected, individuals are usually contagious starting the day before symptoms appear and continuing for about 5-7 days. For most people, influenza is mild and self-limiting, with symptoms lasting up to 2 weeks. Individuals infected with influenza often report a sudden onset of symptoms including fever, chills, cough, sore throat, rhinorrhea, nasal congestion, muscle or body aches, headache, and fatigue (See the Patient Connection for a symptom comparison to the common cold). Complications may include pneumonia, ear infections, sinus infections, and exacerbations of existing medical conditions (including asthma, heart disease, and diabetes). See Table 1 for a list of individuals at high risk for complications.

Diagnosis
Viral testing is not necessary to diagnose influenza. Clinicians can often make a diagnosis based on an evaluation of symptoms, clinical judgement, and local influenza activity. However, diagnostic testing can be used if it will guide decisions to start medications or perform other diagnostic tests, or will impact infection control measures (eg, in a skilled nursing facility). The diagnostic tests used to detect influenza virus in respiratory secretions include molecular assays (rapid molecular assays, reverse transcription polymerase chain reaction [RT-PCR], nucleic acid amplification tests), antigen detection tests (rapid influenza diagnostic tests [RIDTs], immunofluorescence assays), and viral cultures (used for public health purposes). RIDTs are the most common diagnostic tests (used in medical offices or pharmacies) and can produce results within 10-15 minutes. In contrast, a RT-PCR test takes 45 minutes to several hours. RIDTs work by detecting influenza virus antigens in respiratory specimens (from nasal or throat swabs). Respiratory specimens should be collected as early as possible, and not more than 5 days after symptom onset.

Influenza Vaccines
Composition
The composition of the flu vaccine is reviewed and updated annually to match the virus strains anticipated to be circulating in the upcoming season. Based on recommendations from the World Health Organization, (and as is usually the case), the 2018-2019 season trivalent vaccines contain 2 influenza type A strains (H1N1 and H3N2) and 1 influenza type B strain. Quadrivalent vaccines will contain an additional B strain. Adding a second B strain helps with the difficulty of predicting which circulating B lineage will predominate during a season. Providers should anticipate a limited amount of trivalent vaccine in 2018–2019, as the vaccine market is shifting towards quadrivalent vaccines. Flu vaccines will not protect against infection and illness caused by viruses other than those included in the formulation.
Effectiveness
The CDC conducts vaccine effectiveness (VE) studies using data from the US Flu Vaccine Effectiveness Network to assess the value of influenza vaccination. VE can vary each season and depends on 2 factors: characteristics of the recipient (such as age and medical conditions) and the similarity (or “match”) of the vaccine to the circulating strains in the community. In general, influenza vaccine is less effective against influenza A(H3N2) viruses, in patients with chronic medical conditions, the elderly, and in seasons with a mismatch. Since 2004, the adjusted overall VE has ranged from 10% to 60%. For the 2017-18 season, estimates of the overall adjusted VE against influenza A and B are approximately 36%. The VE by strain was 25% against influenza A(H3N2), 67% against influenza A(H1N1), and 42% against influenza B. Overall, the 2017-2018 formulation reduced the risk of getting sick with the flu by about one-third; however, it was much more effective against influenza A(H1N1) and influenza B viruses than the A(H3N2) strain. Generally, patients who received the vaccine and still got the flu had fewer symptoms or less severe symptoms than they would have if they had not received the vaccine.

Practical Considerations in Vaccine Selection
There are 2 types of influenza vaccine available in the US: inactivated influenza vaccine (IIV), also called the “flu shot,” and live attenuated influenza vaccine (LAIV). Approved age indications, dosage, routes of administration, adverse effects, and precautions/contraindications vary by manufacturer and product. The ACIP does not have a preference for one specific IIV product. Any licensed, age-appropriate vaccine can be used, starting before the onset of influenza activity and continuing until unexpired vaccine is no longer available. Vaccination should not be delayed if a specific product is not currently available. Expanded coverage with quadrivalent vaccines may be beneficial among children and at-risk populations, and when there is a mismatch between the trivalent vaccine and circulating influenza B strains. Patients who have received 1 vaccine (for example, the trivalent or high-dose vaccine) should not receive a second immunization with another vaccine product (for example, quadrivalent or adjuvanted vaccine) in the same season. The controversy regarding the use of LAIV and its new recommendations, are discussed on page 6.

Inactivated influenza vaccines (IIVs) contain split-virus and subunit inactivated virus. The antigen load resulting from these viral components, which do not replicate or cause illness, is what stimulates an immune response. IIVs are available in a variety of preparations including:

- Standard-dose (SD-IIV) – manufactured using viruses grown in chicken eggs; multiple products from different manufacturers
- High-dose (HD-IIV3; Fluzone High-Dose®) – contains 4 times as much influenza A surface antigen hemagglutinin (HA) as the standard-dose formulation
- Adjuvanted (allV3; Fluad®) – manufactured using an egg-based process and formulated with the adjuvant MF59 (an oil-in-water emulsion of squalene oil)

Note: Individuals 65 years of age and older generally have a reduced ability to generate an antibody response following vaccination. To address this issue, both the high dose and adjuvanted vaccines are formulated with added contents (eg, HA, squalene oil emulsion) to induce a significantly higher antibody response compared to a standard-dose vaccine. However, it isn’t clear which is more effective; there are currently no studies directly comparing high-dose with adjuvant vaccines.
<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosage Form</th>
<th>Age Indications</th>
<th>Dose and Route</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IIV4 - Inactivated influenza vaccine, Quadrivalent; Standard-Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afluria Quadrivalent*</td>
<td>0.5 mL PFS</td>
<td>≥ 5 years</td>
<td>0.5 mL IM IM</td>
<td>preservative free</td>
</tr>
<tr>
<td></td>
<td>5 mL MDV</td>
<td>≥ 5 years (by needle) 18-64 years</td>
<td>or jet injector</td>
<td>contains 24.5 µg/0.5 mL thimerosal</td>
</tr>
<tr>
<td></td>
<td>0.5 mL PFS</td>
<td>≥ 6 months</td>
<td>0.5 mL IM</td>
<td>preservative free</td>
</tr>
<tr>
<td></td>
<td>PFS 5 mL MDV</td>
<td>≥ 6 months</td>
<td>0.5 mL IM</td>
<td>PFS is preservative free; MDV contains &lt; 25 µg/0.5 mL thimerosal</td>
</tr>
<tr>
<td></td>
<td>0.25 mL PFS</td>
<td>6-35 months</td>
<td>0.25 mL IM</td>
<td>PFS and SDV are preservative free; MDV contains 25 µg/0.5 mL thimerosal</td>
</tr>
<tr>
<td></td>
<td>0.5 mL PFS</td>
<td>≥ 3 years</td>
<td>0.5 mL IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5 mL SDV</td>
<td>≥ 3 years</td>
<td>0.5 mL IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 mL MDV</td>
<td>≥ 6 months</td>
<td>0.25 mL (6-35 months) IM; 0.5 mL (≥ 3 years) IM</td>
<td></td>
</tr>
<tr>
<td><strong>IIV4 - Inactivated influenza vaccine, Quadrivalent; Reduced-Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluzone Intradermal Quadrivalent*</td>
<td>0.1 mL PFS</td>
<td>18-64 years</td>
<td>0.1 mL ID</td>
<td>PFS is a microinjection system, preservative free</td>
</tr>
<tr>
<td><strong>IIV3 - Inactivated influenza vaccine, Trivalent; High-Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluzone High-Dose*</td>
<td>0.5 mL PFS</td>
<td>≥ 65 years</td>
<td>0.5 mL IM</td>
<td>preservative free</td>
</tr>
<tr>
<td><strong>aIIV3 - Adjuvant, inactivated influenza vaccine, Trivalent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluad*</td>
<td>0.5 mL PFS</td>
<td>≥ 65 years</td>
<td>0.5 mL IM</td>
<td>tip cap may contain latex; preservative free</td>
</tr>
<tr>
<td><strong>cclIV4 - Cell-cultured, inactivated influenza vaccine, Quadrivalent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flucelvax Quadrivalent*</td>
<td>0.5 mL PFS</td>
<td>≥ 4 years</td>
<td>0.5 mL IM</td>
<td>tip cap of PFS may contain latex; preservative free; MDV contains 25 µg/0.5 mL thimerosal</td>
</tr>
<tr>
<td><strong>RIV4 - Recombinant influenza vaccine, Quadrivalent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flublok Quadrivalent*</td>
<td>0.5 mL PFS</td>
<td>≥ 18 years</td>
<td>0.5 mL IM</td>
<td>preservative free</td>
</tr>
<tr>
<td><strong>LAIV4 - Live attenuated influenza vaccine, Quadrivalent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FluMist Quadrivalent*</td>
<td>0.2 mL Nasal spray</td>
<td>2-49 years</td>
<td>0.1 mL in each nostril (0.2 mL total)</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations: IM, intramuscular; MDV, multidose vial; PFS, prefilled syringe; SDV, single dose vial*
**Live attenuated influenza vaccines (LAIV)** contain weakened (attenuated) virus that is cold-adapted and grown in chicken eggs. The attenuated virus strains in the vaccine are alive, but less virulent.\(^1\) They do not cause influenza. *Flumist® Quadrivalent*, which is administered intranasally, is currently the only available LAIV product. Over the last few years, recommendations for the use of LAIV have fluctuated widely. In the 2014-2015 season, the ACIP recommended LAIV for young children; however, the ACIP returned to a non-preferential stance in the 2015-2016 season.\(^23,24\) Then, for the 2016 through 2018 seasons, the ACIP recommended against the use of LAIV due to evidence of reduced efficacy compared with IIV.\(^6,25\) The VE was lower for LAIV compared to IIV in children 2-17 years old for 3 consecutive flu seasons (2013 through 2016). In the 2015-2016 season, the VE of LAIV against the H1N1 strain in this population was only 3%, compared to 63% for IIV.\(^7\) One possible explanation for the poor effectiveness of LAIV against A(H1N1) is the strain included in the vaccine.\(^26\)

For the 2018-2019 flu season, a new H1N1 strain (A/Slovenia) will replace the A(H1N1)/Bolivia strain. Although several studies are still ongoing, the A/Slovenia strain showed improved protection when compared with previous LAIV strains. Other clinical trials have shown that a VE of 45% for the new LAIV was comparable to that of IIV.\(^27,28\) Based on the manufacturer’s change in LAIV formulation and other public health concerns, the ACIP voted to include the use of LAIV as an option for the upcoming season.\(^29\) Despite the ACIP recommendation, the American Academy of Pediatrics (AAP) recommends against the use of LAIV in children for 2018-2019 except as a last option, due to poor VE in previous years and unknown effectiveness in the coming season.\(^30,31\)
Dosage in Children
One annual dose of influenza vaccine is recommended for all individuals aged 6 months and older, using an age-appropriate vaccine. However, children aged 6 months to 8 years old should receive 2 doses, spaced at least 4 weeks apart, during their first season of vaccination. See Figure 1 for an algorithm for this recommendation. Available vaccine products with age indications, dosage, and routes of administration can be found in Table 2.

Safety
The most common side effects of IIV are injection-site reactions (15-20%), such as soreness, redness, tenderness, or swelling. Systemic side effects (less than 1%), such as low-grade fever, headache, malaise or muscle aches, are less common and may be more likely to occur in persons with no previous exposure to vaccine antigens. These reactions are often mild (not interfering with activity) and self-limiting, lasting 1-2 days after injection.

Side effects are more frequent with HD-IIV, while intra-dermal IIV causes less pain and bruising but is linked with more local inflammatory reactions and muscle aches. LAIV has slightly higher rates of systemic side effects, which may also include rhinorrhea, nasal congestion, sore throat, or fever. Quadrivalent and trivalent vaccines have similar safety profiles.

Allergic or hypersensitivity reactions to influenza vaccines are rare. Symptoms can range from hives to angioedema or anaphylaxis. The only universal contraindication across all vaccine products is a history of severe allergic reaction to any vaccine component (including latex, which may be in the packaging of certain flu vaccines) or after a previous dose. See Table 3 for a detailed list of influenza vaccine precautions and contraindications.

Among more than 7.4 million doses of IIV vaccine administered in 2015, there were only 10 cases of anaphylaxis (approximately 1.35 per million doses) and most of these were not due to the egg protein in the vaccine. Additionally, a compilation of studies with 4,315 egg-allergic patients found no cases of anaphylaxis as a result of receiving an egg-based IIV. Because of this data, the ACIP updated its guidelines in 2016 to remove restrictions on administration of influenza vaccines to persons with egg allergy. Any licensed, age-appropriate vaccine can be administered to persons with egg allergy of any severity, with a 15-minute post-vaccination observation period. Individuals with a history of severe allergic reaction to egg (any symptom other than hives) should be vaccinated in a medical setting under the supervision of a provider who is able to identify and manage severe allergic conditions.

Figure 1. Dosing Algorithm for Children Less Than 9 Years

<table>
<thead>
<tr>
<th>Have 2 or more doses of the influenza vaccine been received prior to the current season?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, 2 or more doses have been received (either in the same or consecutive seasons).</td>
</tr>
<tr>
<td>No or unsure.</td>
</tr>
</tbody>
</table>

- Administer 1 dose of the current season’s influenza vaccine.
- Administer 2 doses (at least 4 weeks apart) of the current season’s influenza vaccine.
Influenza Antiviral Medications

There are currently 5 antiviral medications available in the US: oseltamivir, zanamivir, peramivir, amantadine, and rimantadine.\(^1\) (See Table 4.) The use of amantadine or rimantadine is no longer recommended due to increasing resistance of circulating influenza A virus strains.\(^35\) Antiviral medications may be used for treatment of influenza or for prevention.

**Treatment** - In deciding to use antivirals for treatment, clinicians should consider flu severity and progression, age, other medical conditions, and time since onset of symptoms. Weight, kidney function, and the potential for drug-drug interactions should also be evaluated.\(^35\)

Treatment should be initiated as soon as possible (preferably within 48 hours of symptom onset) if influenza is suspected (with or without diagnostic testing), especially if the patient is at high risk for complications, has severe, complicated, or progressive disease, or is hospitalized.\(^35,36\)

Individuals who may benefit from antiviral medications include:
- children younger than 2 years of age
- adults aged 65 years and older
- persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), kidney, liver, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopmental conditions (eg, disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy, or stroke)
- persons with immunosuppression, including that caused by medications or by HIV infection
- women who are pregnant or postpartum (within 2 weeks after delivery)
- persons younger than 19 years of age who are receiving long-term aspirin therapy

Early antiviral treatment shortens the duration of fever and other symptoms by 1 or 2 days, lowers the risk of flu complications and death in hospitalized adult patients, and shortens the duration of hospitalization in children.\(^36\)

**Prevention** - The use of antivirals is not a replacement for vaccination when vaccines are available. Pre-exposure (or seasonal) and post-exposure chemoprophylaxis with anti-viral medications is not routinely recommended. However, chemoprophylaxis can be considered for the following populations who have been exposed to the virus:\(^35,36\)
- High-risk individuals (see Table 1) during the first 2 weeks after vaccination, or those who cannot receive the vaccine due to a contraindication

---

Table 3. Influenza Vaccine Precautions & Contraindications\(^6\)

<table>
<thead>
<tr>
<th>Precautions</th>
<th>Contraindications</th>
</tr>
</thead>
</table>
| All vaccines | • History of severe allergic reaction to any component of the vaccine  
• History of severe allergic reaction after a dose of any influenza vaccine |
| Additional precautions and contraindications for LAIV | • Asthma in persons 5 years of age or older  
• Other underlying medical conditions that might predispose to complications after wild-type influenza infection (eg, chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [eg, diabetes mellitus])  
• Concurrent ASA or salicylate-containing therapy in children and adolescents  
• Children aged 2-4 years old who received a diagnosis of asthma or who have a history of wheezing or asthma during the preceding 12 months  
• Children and adults who are immunocompromised due to any cause (including immunosuppression caused by medications or HIV infection)  
• Close contacts and caregivers of severely immunosuppressed persons who require a protected environment  
• Pregnancy  
• Receipt of influenza antiviral medication within the previous 48 hours |

Abbreviations: ASA, aspirin; HIV, human immunodeficiency virus; LAIV, live attenuated influenza vaccine
Table 4. Antiviral Medications

<table>
<thead>
<tr>
<th>Medication (route)</th>
<th>Chemoprophylaxis</th>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir (Tamflu®) Oral</td>
<td>Duration: 7 days (after last known exposure), initiated within 48 hours of close contact with infected person) Dosing Infants 3-11 months (off-label): 3 mg/kg daily Children 1-12 years: ≤ 15 kg: 30 mg daily &gt; 15-23 kg: 45 mg daily &gt; 23-40 kg: 60 mg daily &gt; 40 kg: 75 mg daily Adults / children ≥ 13 years: 75 mg daily</td>
<td>Duration: 5 days Dosing Infants 2 weeks - 11 months old: 3 mg/kg BID Children 1-12 years old: ≤ 15 kg: 30 mg twice daily &gt; 15-23 kg: 45 mg twice daily &gt; 23-40 kg: 60 mg twice daily &gt; 40 kg: 75 mg twice daily Adults / children ≥ 13 years: 75 mg BID</td>
<td>• Dose adjustments required for kidney impairment; use is not recommended in patients with end stage kidney disease unless undergoing dialysis • Efficacy has not been shown in children 6-12 years old with asthma • Better-tolerated if taken with food • Contains sorbitol and may cause stomach upset and diarrhea in people who are fructose (fruit sugar) intolerant • Common side effects: nausea and vomiting (mainly during first 2 days), headache, bronchitis, insomnia, and dizziness</td>
</tr>
<tr>
<td>Zanamivir (Relenza®) Inhaled</td>
<td>Duration: 7 days if initiated within 36 hours of close contact with infected person Dosing Children 5 years and older and adults: 10 mg (two 5 mg inhalations) daily</td>
<td>Duration: 5 days Dosing Children 7 years and older and adults: 10 mg (two 5 mg inhalations) twice daily</td>
<td>• Not recommended for persons with underlying airway diseases, such as asthma or COPD (risk of bronchospasm) • Not shown to be effective for prevention in the nursing home setting • No dose adjustment needed for kidney impairment • Common side effects: sinusitis, dizziness, fever and/or chills, muscle and joint pain</td>
</tr>
<tr>
<td>Peramivir (Rapivab®) Intravenous</td>
<td>N/A</td>
<td>Duration: single dose infused over at least 15 minutes Dosing Children 2-12 years: 12 mg/kg (up to 600 mg) Adults / children ≥ 13 years: 600 mg</td>
<td>• Duration of treatment is 1 day • Common side effect: diarrhea</td>
</tr>
</tbody>
</table>

• Patients who are severely immunocompromised and may not respond to vaccination.

In an institutional outbreak, chemoprophylaxis should be taken daily for the duration of the potential exposure and continued for 7 days after the last known exposure. Following vaccination, continue prophylaxis until immunity from the vaccination has developed (about 2 weeks).35,36 Patients who are receiving chemoprophylaxis should also seek medical care as soon as influenza is suspected.

Summary

All healthcare providers can play a key role in promoting and maintaining high immunization rates. Encourage all individuals and their families to be vaccinated before the flu season starts (or at any time during the season if they haven’t yet been vaccinated). Staying current on new influenza developments, including new vaccine and anti-viral drug products and expert recommendations, is critical for guiding patients, care givers, and other providers.

Chief Editor: Terry M. Baker, PharmD; Managing Editor: Tracy Farnen, PharmD; Associate Editors: James Chan, PharmD, PhD, Cherie Dillon, PharmD, Nina Escasa, PharmD, BCPs, Ron Finley, RPh, Angie Graham, PharmD, Julio R. Lopez, PharmD, FCSHP, Pamela Mausner, MD, Senior Editorial Advisor: Gerard Hatheway, PharmD, PhD; Editorial Advisors: Helen Berlie, Pharm.D., CDE; Belinda M. Danielson, RPh, Christopher M. DeSoto, PharmD; Fred S. Mayer, RPh, MPH, Fred Plageman, PharmD; Editorial Advisor & Clinical Practice Consultant for Nurse Practitioners: Emily K. Meuleman, MS, FNP-BC; Continuing Education Coordinator: Ashrani Chandra
References


Exam Questions:

1. Which of the following regarding influenza is a true statement?
   A. Influenza symptoms usually last for 3-4 weeks.
   B. The time between exposure to influenza and onset of symptoms ranges from 7 to 10 days.
   C. Infected persons are typically contagious a day before symptom onset and for 2 weeks thereafter.
   D. Infected persons are typically contagious a day before symptom onset and for 5-7 days thereafter.

2. Which of the following is a usual symptom of influenza?
   A. Gradual onset of sore throat and nasal congestion
   B. Sneezing and watery eyes
   C. Abrupt onset of fever and muscle aches (often severe)
   D. Gradual onset of headache and fatigue

3. Which of the following persons is more likely than the others to develop severe complications from influenza?
   a. A 55 year old man with COPD
   b. A 40 year old woman who has recently had shoulder surgery
   c. An athletic teenager who spends a lot of time in the gym
   d. A woman who delivered a baby just before the flu season

4. Which of the following is true of rapid influenza diagnostic tests (RIDTs)?
   a. RIDTs usually take 60-90 minutes to produce a result.
   b. RIDTs are required to make the diagnosis of influenza.
   c. Specimens to be tested should be obtained as soon as possible.
   d. Blood from fingersticks is the most common specimen used for RIDTs.

5. Which of the following helps determine vaccine effectiveness?
   A. Climate or environmental conditions where the vaccine is given.
   B. Number of people in the community who receive the vaccine.
   C. Weight and gender of the recipients.
   D. Similarity of the vaccine strains to circulating strains in the community.

6. What should you tell a patient who says he is not getting a flu shot this year because last year it did not work?
   a. This year's flu vaccine is predicted to be twice as effective as last year's.
   b. Even if the vaccine is less effective than desired, patients who are vaccinated and still get the flu will have fewer symptoms or less severe symptoms than had they not received the vaccine at all.
   c. Last year, the strains included in the vaccines were affected by the manufacturing process; this year a different technology will be used.
   d. Despite low effectiveness of the vaccine last year, fewer people than in previous years contracted the flu.
7. Which influenza vaccine is best suited for patients ≥ 65 years old?
A. FluBlok®
B. FluMist® Quadrivalent
C. Fluzone® Intradermal
D. Flua®

8. The ACIP recommends that LAIV (Flumist®) be an influenza vaccination option in 2018-2019. Why might it still be underused?
A. The American academy of Pediatrics is recommending against its use as a first line option.
B. The cost of the formulation is considerably greater than prefilled syringes.
C. The needleless jet injector system for the Afluria® Quadrivalent vaccine will be preferred over the LAIV.
D. LAIV is now contraindicated in younger patients (under the age of 18 years).

9. The parent of a 3 year old is unsure if the child received 2 doses of the influenza vaccine before. What should you do?
A. Offer 2 doses of this season's current vaccine at least 2 weeks apart.
B. Offer 2 doses of this season's current vaccine at least 4 weeks apart.
C. Let the child's pediatrician know that he or she needs the LAIV vaccine.
D. Offer the child a quadrivalent vaccine followed by a trivalent vaccine at least 4 weeks apart.

10. What type of patient is more likely to experience systemic side effects of influenza vaccines?
A. A person who has preexisting kidney disease.
B. Older persons who have not received a quadrivalent influenza vaccine.
C. A person who has an allergy to eggs.
D. A person who has not previously been exposed to vaccine antigens.

11. Which of the following is true regarding the use of antiviral medications for treating influenza?
A. All influenza vaccines can be administered during antiviral treatment.
B. Antiviral agents should be administered as soon as possible in high risk populations as long as diagnostic testing confirms an influenza infection.
C. Peramivir should be given intravenously once daily for 5 days.
D. Zanamivir should NOT be administered to people with COPD or asthma.

12. Which of the following individuals is a candidate for chemoprophylaxis with an antiviral?
A. A 3rd grade student who attends a school where there is a flu outbreak
B. An elderly person over the age of 75 years
C. An immunocompromised cancer patient living with his granddaughter who has the flu
D. A stay-at-home mom whose husband has the flu