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HealthLine

Focus on Seasonal Influenza 2017–2018

- by Allen Lefkovitz

According to the National Center for Health Statistics, influenza and pneumonia are the 8th leading cause of death in the United States. The Centers for Disease Control and Prevention (CDC) define "influenza-like illness" as a fever [oral temperature ≥ 100.0˚F (≥ 37.8˚C) or equivalent] and a cough and/or sore throat without a known cause other than influenza. The highest rates of severe illness and influenza-associated hospitalizations occur in older adults (i.e., individuals 65 years of age and older) and in children less than 2 years old. For various reasons, influenza vaccine effectiveness is typically lowest in older adults. In 2016-2017, nearly 32% of influenza cases reported were in older adults. From October 1, 2016 through April 30, 2017, over 18,000 hospitalizations related to influenza were reported, of which approximately 60% involved older adults. It is also noteworthy that a CDC survey of older adults found that in 2015 only 69% reported receiving an influenza vaccine in the preceding 12 months.

The Advisory Committee on Immunization Practices (ACIP) continues to recommend **routine annual influenza vaccination for everyone 6 months of age or older unless otherwise contraindicated**. The 2016-17 influenza season was classified as "moderate" overall by CDC. Interim data suggest that the 2016-2017 influenza vaccines were only 48% effective, but CDC points out that "Even during seasons when vaccine effectiveness is reduced, vaccination can offer substantial benefit and reduce the likelihood of severe outcomes such as hospitalization and death." According to the most recent CDC estimates, influenza vaccination during the 2015-2016 season prevented:

- 5.1 million influenza illnesses
- 71,000 influenza-associated hospitalizations, and
- 3,000 pneumonia and influenza deaths.

Highlights from the 2017-2018 ACIP Recommendations

Recognizing that it takes about 2 weeks to develop the necessary antibodies, ACIP states that "Optimally, vaccination should occur before onset of influenza activity in the community. Health care providers should offer vaccination **by the end of October**, if possible." Additionally, they recommend that "Vaccination should continue to be offered as long as influenza viruses are circulating and unexpired vaccine is available."

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Inside This Issue

The variety of influenza vaccines continues to expand. Available products include:

- standard- and high-dose formulations
- trivalent and quadrivalent formulations
- formulations grown in eggs, recombinant "egg-free" formulations, and formulations grown in cell cultures
- adjuvanted and non-adjuvanted formulations.

A summary of the available influenza vaccines for 2017-2018 is on page 3.

The composition of this season's trivalent and quadrivalent influenza vaccines are described below:

The 2017–2018 Trivalent vaccine (A+A+B)
A/Michigan/45/2015 (H1N1)-like virus +
A/Hong Kong/4801/2014 (H3N2)-like virus +
B/Brisbane/60/2008-like (Victoria lineage) virus

The 2017–2018 Quadrivalent vaccine (A+A+B+B)
The 3 components of the Trivalent vaccine (above)
B/Phuket/3073/2013-like (Yamagata lineage) virus

Since the 2009 pandemic (aka "swine") influenza outbreak, every influenza vaccine has included A/California/7/2009 (H1N1)-like virus; however, based upon more recent surveillance, the 2017-2018 vaccines have changed to A/Michigan/45/2015 (H1N1)-like virus in order to help combat newly emerging strains of influenza.

Since the publication of last year's recommendations, two new products were approved:

- Afluria Quadrivalent for those 18 years of age and older
- Flublok Quadrivalent for those 18 years of age and older [available in addition to the original trivalent Flublok]

Changes/important notes for previously approved products include the following:

- FluLaval Quadrivalent is now approved for children as young as 6 months (instead of only 3 years and older); this represents a second option for children 6 months to 3 years of age
- Afluria may be used in anyone 5 years or older [previously ACIP had limited use to children 9 years or older due to data suggestive of increased seizure risk]
- Live attenuated influenza vaccine [(LAIV) i.e., FluMist] remains as not recommended for use during the 2017-2018 season (due to effectiveness concerns). While it is still FDA approved and can be prescribed, use of LAIV would be contrary to CDC recommendations.

Which vaccine is preferred?

All formulations except Fluzone Intradermal and FluMist Quadrivalent are approved for use in older adults. ACIP recommendations continue to state "A licensed, recommended, and age-appropriate vaccine should be used", as opposed to recommending one vaccine over another. Likewise, CDC warns against delaying vaccination in order to obtain a specific formulation if another appropriate alternative is available.

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Trade Name	Manufacturer	Contains Mercury?	Approved Age Group
Trivalent, Inactivated Influenza Vaccine (IIV3)			
Alfuria®	Seqirus	Only in MDV	≥ 5 years*†
Fluvirin®	Seqirus	Yes‡	≥ 4 years
Fluzone® High-Dose	Sanofi Pasteur	No	≥ 65 years
Trivalent, Inactivated Influenza Vaccine (aIIV3) with Adjuvant (MF-59®)			
Fluad™	Seqirus	No‡	≥ 65 years
Trivalent, Recombinant Influenza Vaccine (RIV3)			
Flublok®	Protein Sciences	No	≥ 18 years
Quadrivalent, Inactivated Influenza Vaccine (IIV4)			
Alfuria® Quadrivalent	Seqirus	Only in MDV	≥ 18 years†
Fluarix® Quadrivalent	GlaxoSmithKline	No	≥ 3 years
FluLaval® Quadrivalent	ID Biomedical	Only in MDV	≥ 6 months
Fluzone® Quadrivalent	Sanofi Pasteur	Only in MDV	≥ 3 years§
Fluzone® Intradermal Quadrivalent	Sanofi Pasteur	No	18–64 years
Quadrivalent, Cell Culture-based Inactivated Influenza Vaccine (ccIIV4)			
Flucelvax® Quadrivalent	Seqirus	Only in MDV	≥ 4 years
Quadrivalent, Recombinant Influenza Vaccine (RIV4)			
Flublok® Quadrivalent	Protein Sciences	No	≥ 18 years
Quadrivalent, Live Attenuated Influenza Vaccine (LAIV4) Intranasal (Not recommended for use)			
FluMist® Quadrivalent	MedImmune	No	2–49 years

MDV=Multiple-dose vials
*Trivalent Alfuria is a FDA approved for those ≥ 5 years. ACIP no longer limits use to those 9 years or older.
† Alfuria and Alfuria Quadrivalent may also be given using a jet injector for patients 18 to 64 years of age.
‡Prefilled syringes have a tip cap that may contain natural rubber latex.
§ The multiple-dose vials are approved for ≥ 6 months, but single-dose 0.5mL vials and syringes are only approved for ≥ 3 years. A smaller 0.25 mL prefilled syringe is available for use in children 6 to 35 months.

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Although not relevant to older adults, another change in the ACIP recommendations is that pregnant women may now receive any licensed, recommended, age-appropriate influenza vaccine and it can be administered at any time during pregnancy (before and during the influenza season). Previously, data were limited in the early first trimester of pregnancy. CDC will continue to monitor the safe use of influenza vaccines in pregnancy through their surveillance of pregnancy registries and the Vaccine Adverse Event Reporting System (VAERS). Additionally, for children ages 6 months to 8 years, 2 doses of the 2017-2018 influenza vaccine should be administered (at least 4 weeks apart) UNLESS they have received 2 or more doses during any previous season.

Allergies and Influenza Vaccination
CDC generally suggests that if a person reports history of a severe allergy (e.g., anaphylaxis) to any known substance contained in a vaccine, an alternative vaccine that does not contain that substance should be considered instead of complete avoidance of vaccination. However, a previous severe allergic reaction to an actual influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine.

Except for recombinant influenza vaccines [(RIV3 or RIV4), i.e., Flublok and Flublok Quadrivalent] and cell culture-based inactivated influenza vaccine [(ccIIV4), i.e., Flucelvax], all influenza vaccines are made by growing viruses in embryonated chicken eggs; however, even ccIIV4 contains a very small amount of egg protein, such that only Flublok and Flublok Quadrivalent are deemed completely "egg-free".

First changed for the 2016-2017 season, ACIP has provided specific guidance that anyone with a history of severe allergic reaction to eggs (i.e., more than hives) now may receive any recommended and age appropriate influenza vaccine, but they should be vaccinated only in an inpatient or outpatient medical setting under the supervision of a healthcare provider who is able to recognize and manage severe allergic conditions. Also continued from last season's recommendations is that everyone vaccinated (regardless of allergies) should be monitored for 15 minutes after vaccination to watch for allergic reaction and to decrease the risk of injury due to syncope.

Antiviral Medications for Influenza
Older antiviral medications (i.e., amantadine and rimantadine) have not been recommended since 2011 due to increased influenza A virus resistance and ineffectiveness against influenza B virus. Neuraminidase inhibitors for chemoprophylaxis and treatment [i.e., Tamiflu (oseltamivir) capsules and Relenza (zanamivir) inhaler] as well as an intravenous option [i.e., Rapivab (peramivir)] for influenza treatment have been available for several years. During the 2016-2017 season, generic oseltamivir (Tamiflu) capsules became available. CDC reported for 2016-2017 that all virus samples tested were susceptible to all three newer antiviral medications (i.e., oseltamivir, zanamivir, and peramivir).

According to CDC "Early treatment with neuraminidase inhibitor antiviral medications is recommended for patients with severe, complicated, or progressive influenza illness and those at higher risk for influenza complications, including adults aged ≥ 65 years." Additionally, CDC recommends that prescribers consider the prophylactic use of antiviral medications for individuals who are medically unable to receive influenza vaccination. Additional information on oral antiviral medications for treatment and prevention of influenza can be found in the Clinical Capsule on page 7.

Influenza Vaccination and Long-Term Care (LTC)
When the changes to the State Operations Manual Appendix PP – Guidance to Surveyors for LTC Facilities become effective on November 28, 2017, what was previously F334 will become F883 – Influenza and pneumococcal immunizations. Facilities must continue to have policies and procedures in place that ensure:

- each resident or their representative receives education about the benefits and potential side effects of the immunization;
- influenza immunization is offered between October 1 through March 31, unless the immunization is medically contraindicated or they have already been immunized;
- the resident or their representative has the opportunity to refuse immunization; and
- the resident's medical record includes, at a minimum, documentation of the aforementioned education and that the resident either received the influenza vaccine or did not receive it due to a medical contraindication or refusal.

An important clarification within F883 is that unlike with other vaccinations, self-reported history of vaccination for

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only influenza or pneumococcal polysaccharide vaccine [(PPSV23), i.e., Pneumovax 23] is acceptable (unless state laws have more stringent requirements related to documentation).

The revisions to F883 also reinforce that "CDC indicates that administering the vaccine when it becomes available each season, rather than date specific (i.e., "October 1") is most effective. Facilities should administer the influenza vaccine when it becomes available to the facility."

Another new area addressed in F883 is what to do if a national shortage of influenza vaccine or other availability issues arise. Although supplies of influenza vaccine are believed to be sufficient for this year, in the event of a shortage or availability issue, facilities must demonstrate that they have taken the necessary steps to try to obtain the vaccine and they must have their plans, screening, and education already in place.

ACIP recommendations include all residents of nursing homes and other LTC facilities as individuals who are at higher risk for influenza-related complications. Nursing Home Compare data currently indicate that 94.7% of long-stay residents and 80.2% of short-stay residents who "needed" an influenza vaccine received it. In addition to the residents, attention must also be given to those who have direct contact with them. For this reason, ACIP also recommends that vaccination be emphasized for "employees of nursing home and long-term care facilities who have contact with patients or residents, and students…who will have contact with patients". Utilizing the most recent information from the 2015-2016 season, CDC says that influenza vaccine coverage of all healthcare personnel (HCP) increased slightly to 79.0%. While vaccination among LTC personnel was the only area in healthcare where vaccination rates increased significantly (from 63.9% in 2014-2015 to 69.2% in 2015-2016), LTC remains the area of lowest vaccination among HCP.

To encourage vaccination among healthcare personnel in LTC, CDC continues to provide for free "A Toolkit for Long-Term Care Employers" at: www.cdc.gov/flu/toolkit/long-term-care/.

A summary of the ACIP recommendations and many other helpful influenza resources are available at: **www.cdc.gov/flu/**.

Safe and Proper Administration of Intramuscular Vaccines: Part 1

- by Allen Lefkovitz

This month and next, the medication safety section will overview the safe and proper administration of intramuscular (IM) vaccines. The safe and proper administration of intramuscular (IM) vaccines [e.g., influenza, Prevnar 13 (PCV13)] must be a priority for every healthcare professional (HCP) providing immunizations. Following the administration of any injectable vaccine, the individual should be monitored for adverse effects, including adverse effects related to improper administration.

Risks of improper administration include:

- vaccine ineffectiveness;
- inadvertent needlestick injury;
- shoulder injury related to vaccine administration (SIRVA); and
- radial nerve damage.

Three general principles that can help guide the provision of safe IM vaccinations can be summarized under the categories of Size, Site, and Technique. The topics of Size and Site will be covered this month and an overview of Technique will be covered in next month's issue.

#1: Size

It is important to select the appropriate needle length for proper IM administration of the vaccine.

Patient Characteristics	Recommended Needle Length for IM Injection
Men and women < 130 pounds (< 60 kg)	5/8 - 1 inch
Men and women 130-152 pounds (60-69 kg)	1 inch
Women 153-200 pounds (70-90 kg) Men 153-260 pounds (70-118 kg)	1 - 1 ½ inches
Women > 200 pounds (> 90 kg) Men > 260 pounds (> 118 kg)	1 ½ inches
Children (deltoid administration)	5/8 - 1¼ inches

#2: Site

When selecting which arm to administer the vaccine into, the HCP should consider any history of injury or surgeries in or surrounding the selected arm. Finding an appropriate place to inject in the deltoid muscle is the key to proper and successful vaccine administration. To determine the safest site for injection, the HCP should place 3-5 fingers on the patient's arm or make a "C" shape with their fingers between the top of the shoulder and just below the level of the armpit. The center of this area should be the thickest part of the deltoid muscle (otherwise, reposition the injection). This is done to ensure that the needle passes through the subcutaneous layer and enters the muscle.

- Administering a vaccine too high on the arm may result in swelling, irritation, or SIRVA (e.g., bursitis/shoulder impingement, frozen tendon). SIRVA often occurs within the first 48 hours after vaccination and is associated with pain in the shoulder/vaccinated arm that does not subside and leads to decreased shoulder mobility (either temporarily or permanently).
- Administering a vaccine too low in the arm may result in radial nerve damage, which presents as abnormal sensations in the hand or forearm, difficulty straightening the arm at the elbow, pain, and/or numbness/tingling or decreased or a burning sensation.

Antiviral Agents Used for Influenza Chemoprophylaxis and Treatment

- by Allen Lefkovitz

According to CDC "Early treatment with neuraminidase inhibitor antiviral medications is recommended for patients with severe, complicated, or progressive influenza illness and those at higher risk for influenza complications, including adults aged ≥ 65 years." Older antiviral medications (i.e., amantadine and rimantadine) are not recommended for use. An overview of recommended dosing for the three neuraminidase inhibitors is provided below. The final choice of therapy is a decision that should be made by the prescriber based on individual patient characteristics and the clinical situation. Clinical benefit has been demonstrated when antiviral medications for treatment are initiated early (i.e., within 48 hours of onset of symptoms).

Tamiflu (oseltamivir) Capsule or Suspension Dosing

Estimated Renal Function	Treatment Dose for Adults	Post-Exposure Prophylaxis Dose in LTC*
CrCl > 60 mL/min	75 mg twice daily for 5 days	75 mg once daily for **at least 14 days**
CrCl > 30 - 60 mL/min	30 mg twice daily for 5 days	30 mg once daily for **at least 14 days**
CrCl > 10 - 30 mL/min	30 mg once daily for 5 days	30 mg every other day for **at least 14 days**
ESRD on Hemodialysis (CrCl ≤ 10 mL/min)	30 mg immediately then after dialysis for 5 days	30 mg immediately then after alternate dialysis cycles for **at least 14 days**
ESRD on Continuous Peritoneal Dialysis (CrCl ≤ 10 mL/min)	A single 30 mg dose immediately	30 mg immediately then once weekly after the dialysis exchange for **at least 14 days**

Relenza (zanamivir) Inhalation Dosing†

Treatment Dose for Adults	Post-Exposure Prophylaxis Dose in LTC*
2 inhalations (10 mg) twice daily for 5 days	2 inhalations (10 mg) once daily for **at least 14 days**

Rapivab (peramivir) Intravenous (IV) Dosing‡

Estimated Renal Function	Treatment Dose for Adults
CrCl ≥ 50 mL/min	600 mg x1 dose
CrCl = 30 - 49 mL/min	200 mg x1 dose
CrCl = 10 - 29 mL/min	100 mg x1 dose
ESRD on Hemodialysis	After dialysis at a dose based on renal function

CrCl = creatinine clearance; ESRD = end stage renal disease

* According to the latest guidance from the CDC, within LTC facilities, the recommended minimum length of therapy for prophylaxis is "a minimum of 2 weeks, and continuing up to 1 week after the last known case was identified".
† No dosage adjustment is necessary in patients with renal impairment. However, the potential for drug accumulation should be considered.
‡ Not FDA approved for prophylaxis; should be administered via IV infusion for 15-30 minutes

Additional details are available in the prescribing information for each medication which can be reviewed at: https://dailymed.nlm.nih.gov/.

Baxdela™ Tablets and IV Infusion

- by Dave Pregizer

Brand Name (Generic Name)	**Baxdela™ [bax-de'-lah] (delafloxacin) [del a FLOKS a sin]**
How Supplied	450 mg tablets; 300 mg lyophilized powder in a single dose vial
Therapeutic Class	Fluoroquinolone antibiotic
Approved Indication	Treatment of acute bacterial skin and skin structure infections caused by designated susceptible bacteria in adults (e.g., *Staphylococcus aureus, Streptococcus* sp., *Pseudomonas aeruginosa*)
Usual Dosing	300 mg IV infusion over 60 minutes every 12 hours OR 450 mg orally every 12 hours for 5–14 days (GFR 30–89 mL/min/1.73 m^2: No dose adjustment; GFR 15–29 mL/min/1.73 m^2: 200 mg IV every 12 hours, No dose adjustment orally; GFR < 15 mL/min/1.73 m^2: Not recommended)
Select Drug Interactions	Administer tablet 2 hours before or 6 hours after aluminum or magnesium containing antacids, sucralfate, metal cations such as iron, multivitamins containing iron or zinc, and formulations containing divalent and trivalent cations (interferes with absorption). For the infusion product, do not coadminister any multivalent cations (e.g., calcium, magnesium) through the same IV line.
Most Common Side Effects	Nausea, diarrhea, headache, transaminase elevations and vomiting.
Miscellaneous	Boxed warning for serious adverse reactions including tendinitis and tendon rupture, peripheral neuropathy, central nervous system effects, and exacerbation of muscle weakness with myasthenia gravis. Tablet may be taken with or without food.
Website	www.baxdela.com

GFR = glomerular filtration rate based on the Modification of Diet in Renal Disease (MDRD) equation

NEW Generic Medications

Generic Name	Brand Name	Date Generic Available
Adapalene 0.1% and Benzoyl Peroxide 2.5% Topical Gel	Epiduo® Gel	8/3/17
Scopolamine 1 mg/3 days Transdermal Patches	Transderm Scop® Patch	7/27/17
Eletriptan 20 mg and 40 mg Tablets	Relpax® Tablet	7/25/17
Mesalamine 1.2 g Delayed-Release Tablets	Lialda® DR Tablet	7/18/17

HealthLine Quiz

– by Steve Law

1. **The Advisory Committee on Immunization Practices (ACIP) continues to recommend routine annual influenza vaccination for everyone 6 months of age or older unless contraindicated:**
   a. True b. False

2. **Which statement about influenza vaccines is TRUE:**
   a. Fluzone Intradermal is approved for use in older adults (65 years and older)
   b. It is recommended to give Flumist to a patient who is 40 years old this influenza season
   c. The ACIP recommends using Quadrivalent vaccines over Trivalent vaccines
   d. Pregnant women may now receive an influenza vaccine at any time during pregnancy

3. **For a male patient that weighs 125 pounds, the influenza vaccine should be administered IM with a 1 ½ inch needle:**
   a. True b. False

4. **Renal function needs to be assessed before administering the antiviral medication, Relenza (zanamivir) inhalation:**
   a. True b. Fals

5. **To be in compliance with F883 – influenza and pneumococcal immunizations, which of the following policies and procedures must be in place:**
   a. Each resident or their representative must receive education about the benefits and potential side effects of the immunization
   b. The vaccine should be administered when it becomes available to the facility
   c. The resident or their representative has the opportunity to refuse immunization
   d. In the event of a shortage of vaccine or availability issue, the facility must demonstrate that they have taken necessary steps to try and obtain the vaccine
   e. All of the above

6. **Which statement is FALSE about the new medication, Baxdela™:**
   a. It is a fluoroquinolone antibiotic
   b. It can be given orally or via IV infusion
   c. It has a boxed warning for serious adverse reactions including tendinitis and tendon rupture
   d. Tablets can be administered at the same time as ferrous sulfate

***Please note, the HealthLine Quiz is designed to help readers retain information that is relevant to their care setting. It is not an approved source of continuing education credits for healthcare professionals.**

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Answers to the HealthLine Quiz: 1) A 2) D 3) B 4) B 5) E 6) D