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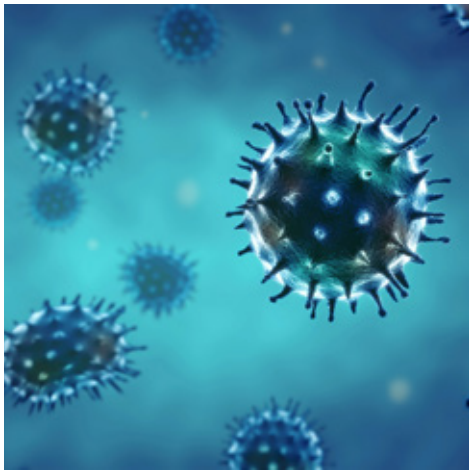
HealthLine

Focus on Seasonal Influenza 2018–2019

- by Allen Lefkovitz

The recent 2017-2018 influenza season has been classified as "a high severity season," associated with the highest overall hospitalization rate ever recorded in the Centers for Disease Control and Prevention (CDC) surveillance system and a higher rate of deaths (compared to the preceding five seasons). However, 2018 is the one hundred year anniversary of the influenza pandemic that killed more than 50 million people globally. Since the 1918 influenza pandemic, research and advances in medicine have led to significant improvements in influenza preparedness, but influenza and pneumonia remain the 8th leading cause of death in the United States. CDC "recommends a yearly flu vaccine as the first and most important step in protecting against influenza and its potentially serious complications." Therefore, since 2010 the Advisory Committee on Immunization Practices (ACIP) has recommended **routine annual influenza vaccination for everyone 6 months of age or older unless otherwise contraindicated.**



Influenza Vaccines for 2018-2019

Although for many years it was the only option available, for 2018-2019, only one manufacturer remains for the standard-dose trivalent influenza vaccine (SD-IIV3); however, other types of influenza vaccines available for this season include:

- multiple standard-dose quadrivalent formulations grown using eggs or cell cultures;
- a high-dose formulation specifically approved for adults 65 years and older;
- an adjuvanted formulation specifically approved for adults 65 years and older; and
- a higher-dose quadrivalent recombinant vaccine.

A summary of the available influenza vaccines for 2018-2019 is on page 2. Changes in regard to vaccine products since the publication of last year's recommendations include:

- Fluzone Intradermal is no longer being manufactured
- Afluria Quadrivalent may be used by those 5 years or older (previously was for 18 years or older)
- Fluarix Quadrivalent may be used by those 6 months or older (previously was for 3 years or older)
- After not recommending its use for the past two influenza seasons, CDC now includes the intranasal, quadrivalent, live attenuated influenza vaccine (LAIV) among other options that may be used for those 2 to 49

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years of age. This change follows reformulation with an improved H1N1 strain intended to produce a greater immune response.

The composition of this season's trivalent vaccine includes two different strains from recent years (i.e., the H3N2 A strain and the B strain). The composition of the trivalent and quadrivalent influenza vaccines are described below:

The 2018–2019 Trivalent vaccine (A + A + B)
A/Michigan/45/2015 (H1N1) pdm09-like virus +
A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus +
B/Colorado/06/2017-like (Victoria lineage) virus

The 2018–2019 Quadrivalent vaccine (A + A + B + B)
The 3 components of the Trivalent vaccine (above) +
B/Phuket/3073/2013-like (Yamagata lineage) virus

Table – Influenza Vaccines Available in 2018-2019

Trade Name	Manufacturer	Contains Mercury?	Approved Age Group
Trivalent, Standard Dose, Inactivated Influenza Vaccine (SD-IIV3)			
Alfuria®	Seqirus	Only in MDV	≥ 5 years*
Quadrivalent, Standard Dose, Inactivated Influenza Vaccine (SD-IIV4)			
Alfuria® Quadrivalent	Seqirus	Only in MDV	≥ 5 years*
Fluarix® Quadrivalent	GlaxoSmithKline	No	≥ 6 months
FluLaval® Quadrivalent	ID Biomedical	Only in MDV	≥ 6 months
Fluzone® Quadrivalent	Sanofi Pasteur	Only in MDV	≥ 3 years†
Quadrivalent, Cell Culture-based, Inactivated Influenza Vaccine (ccIIV4)			
Flucelvax® Quadrivalent	Seqirus	Only in MDV	≥ 4 years
Trivalent, High Dose, Inactivated Influenza Vaccine (HD-IIV3)			
Fluzone® High-Dose	Sanofi Pasteur	No	≥ 65 years
Trivalent, Inactivated Influenza Vaccine with Adjuvant (aIIV3)			
Fluad™	Seqirus	No	≥ 65 years
Quadrivalent, Recombinant Influenza Vaccine (RIV4)			
Flublok® Quadrivalent	Sanofi Pasteur	No	≥ 18 years
Intranasal, Quadrivalent, Live Attenuated Influenza Vaccine (LAIV4)			
FluMist® Quadrivalent	AstraZeneca	No	2–49 years

MDV = Multiple-dose vials
* Afluria and Afluria Quadrivalent may also be given using a jet injector for patients 18 to 64 years of age.
† The multiple-dose vials are approved for ≥ 6 months, but single-dose 0.5 mL 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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Timing of Influenza Vaccine Administration

Because it takes about 2 weeks to develop the necessary antibodies, ACIP states that vaccination efforts should focus on administration of the influenza vaccine "before onset of influenza activity in the community", and they also say "it is recommended that vaccination should be offered **by the end of October**." CDC encourages that "Vaccination efforts should continue throughout the season because the duration of the influenza season varies, and influenza activity might not occur in certain communities until February or March."

CDC also states that IIV3, IIV4, and RIV4 "may be administered concomitantly or sequentially with other inactivated vaccines or with live vaccines", as long as they are administered in separate injection sites. In contrast, individuals administered LAIV4 should wait at least 4 weeks before receiving other live vaccines.

Influenza Vaccines and the Older Adult

Vaccine response may be reduced in older adults due to weakening of their immune system and overall frailty. 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. It is estimated that between 71% and 85% of influenza-related deaths occurred in older adults, and during the 2017-2018 season, older adults accounted for 58% of influenza-associated hospitalizations. Because of this significantly increased risk, influenza vaccine development for older adults remains an area of "active research", and according to CDC this research has primarily revolved around the following 3 vaccines:

Fluzone High-Dose (HD-IIV3)	• This formulation contains four times the amount of each antigen (60 mcg) compared to standard dose trivalent influenza vaccine (15 mcg). • HD-IIV3 has only been studied in comparison to the standard dose, unadjuvanted trivalent vaccine (SD-IIV3). • HD-IIV3 produced significantly higher antibody response and 24% better protection against laboratory-confirmed influenza illness compared to SD-IIV3. • More recently, a meta-analysis showed HD-IIV3 provided better protection against influenza-like illness, pneumonia, cardiorespiratory events, all-cause hospitalizations, and hospitalizations due to influenza.
Fluad (aIIV3)	• This formulation contains an adjuvant (MF59) that helps stimulate or enhance the body's response to the vaccine. • aIIV3 has only been studied in comparison to the standard dose, unadjuvanted trivalent vaccine (SD-IIV3). • In a small single-season observational study, aIIV3 was 63% more effective than unadjuvanted SD-IIV3. Data from a randomized trial are not currently available.
Flublok Quadrivalent (RIV4)	• This formulation contains three times the amount of each antigen (45 mcg) compared to standard dose quadrivalent influenza vaccine (15 mcg). • RIV4 has been studied in comparison to the standard dose, unadjuvanted quadrivalent vaccine (SD-IIV4). • RIV4 was 30% more efficacious than SD-IIV4 in individuals 50 years of age and older and 17% more efficacious in individuals 65 years of age and older; however the Food and Drug Administration currently has not approved any claim of superiority.

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While research into finding a more effective influenza vaccine for older adults continues, CDC recommendations are clear that "**No preference is expressed for any one vaccine type**. Vaccination should not be delayed if a specific product is not readily available. For persons aged ≥ 65 years, any age-appropriate IIV formulation (standard-dose or high-dose, trivalent or quadrivalent, unadjuvanted or adjuvanted) or RIV4 are acceptable options."

Allergies and Influenza Vaccination

CDC generally suggests that if a person reports history of a severe allergy (e.g., anaphylaxis, angioedema) to any known substance contained in a vaccine (e.g., neomycin), 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 any influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the influenza vaccine.

Except for RIV4 (i.e., 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 Quadrivalent is deemed completely "egg-free". Since 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. As a general precaution, vaccinated individuals (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 Treatment and Prophylaxis of Influenza

According to CDC, antiviral treatment is recommended "as early as possible" for older adults as well as residents of nursing homes and other chronic care facilities with confirmed or suspected influenza. CDC also recommends that prescribers consider the prophylactic use of antiviral medications for individuals who are medically unable to receive influenza vaccination. Additionally, CDC states "When influenza is identified as a cause of a respiratory disease outbreak among nursing home residents, use of antiviral medications for chemoprophylaxis is recommended for all non-ill residents (regardless of whether they have received influenza vaccination). Antiviral chemoprophylaxis is meant for residents who are not exhibiting influenza-like illness but who may be exposed or who may have been exposed to an ill person with influenza, to prevent transmission."

Since 2011 older antiviral medications (i.e., amantadine and rimantadine) have not been recommended because of 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. These options remain available for treatment and prophylaxis even though during the 2017-2018 season, 1% of samples tested showed evidence of resistance to commonly utilized antiviral medications. CDC continues to monitor closely the developing risk of resistance to these newer medications.

Additional information on oral antivirals for treatment and prevention of influenza can be found on page 6 of this newsletter.

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Influenza Vaccination and Long-Term Care

ACIP continues to classify all residents of nursing homes and other long-term care facilities (LTCF) as individuals who are at "higher risk for influenza-related complications". Within the State Operations Manual Appendix PP, F883 – "Influenza and pneumococcal immunizations" reinforces 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."

F883 also states that LTCF are expected 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 from October 1 through March 31 annually, 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 distinction within F883 is that unlike with other vaccinations, a self-reported history of vaccination is acceptable for only influenza or pneumococcal polysaccharide vaccine [(PPSV23), i.e., Pneumovax 23] (unless state laws have more stringent requirements related to documentation).

While a national shortage is not anticipated, F883 also states that in the event of a shortage or availability issue, facilities must demonstrate that they have taken the necessary steps to try and obtain the vaccine, and they must have their plans, screening, and education already in place.

Nursing Home Compare data currently indicate that 95.1% of long-stay residents and 81.6% 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 2016-2017 season, CDC says that influenza vaccine coverage of all healthcare personnel (HCP) was 78.6%, slightly lower than the 79.0% in the preceding season. LTCF remain the segment of healthcare with the lowest vaccination rate among HCP at 68.0%. This rate is slightly lower than the 69.2% rate reported in 2015-2016. To encourage vaccination among healthcare personnel in LTCF, 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/**.

Antiviral Agents Used for Influenza Treatment and Prevention

- Allen Lefkovitz and Carrie Allen

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 each dialysis cycle not to exceed 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**
Oseltamivir is not recommended in ESRD patients not undergoing dialysis treatment		

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.
‡ Although FDA approved, Relenza (zanamivir) has not been proven effective for prophylaxis of influenza in the nursing home setting.
§ 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/.

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Our Response to Fulfill the Requirements of the IMPACT Act: A Collaborative Approach

Background

The IMPACT Act stands for the Improving Medicare Post-Acute Care Transformation Act, whose goal is to standardize patient assessment data across several post-acute care settings, including skilled nursing facilities. This Act becomes effective on October 1, 2018, with the release of the new version of the Minimum Data Set, which contains 3 new questions related to Drug Regimen Reviews (DRR). Together the responses to these 3 MDS questions comprise a new Quality Measure called Drug Regimen Review Conducted With Follow-Up For Identified Issues. The IMPACT Act requires that any potential or actual clinically significant medication issues be identified upon, or shortly after, admission of a resident on a Medicare Part A stay. Additionally, the Act stipulates that any identified clinically significant medication issues be resolved by 11:59PM of the next calendar day following issue identification.

Goals

- Assist our skilled nursing facility clients in meeting the new DRR requirements of the IMPACT Act
- Provide education and tools to facilities and prescribers
- Improve the timeliness of the initial medication review, and therefore optimize the safety, quality, regulatory, and cost-effective opportunities for the resident, and for our clients
- Complete a medication review for all new admissions
- Complete a medication regimen review for all residents, independent of their length of stay.

Process

Our dispensing pharmacists review all medications for allergies, drug interactions, duplicate therapies, dosing discrepancies, and other clinical issues for both new admissions and for new orders, and routinely contact facilities to help resolve clinically significant issues in a timely manner.

An off-site consultant pharmacist monitors facility admissions, and, using available information, completes an Admission Medication Review within 72 hours (or agreed upon timeframe) of resident admission. This review may include hospital discharge documents and other information in the facility's electronic health record (EHR), and from our proprietary consulting software program. Any clinically significant medication issues identified during these admission reviews will be communicated to facilities by a consultant pharmacist.

Recommendations made by the consultant pharmacist will be communicated to a facility designee that will be responsible for ensuring prompt follow-up from the prescriber.

Targeted Areas

- Strategies to mitigate risk and fulfill IMPACT Act requirements consist of identification of clinically significant medication issues, review of dosing and monitoring of medications, and reduction of polypharmacy. Additionally, a focus on the appropriate use of antipsychotics, antibiotics, and the elimination or reduction of high-risk medications and duplicate therapies, will occur
- Clinical reviews and recommendations will help optimize care in the areas of diabetes, pain management, COPD, antibiotic stewardship, heart failure, and others
- Cost management strategies include ensuring stop dates for antibiotics and post-operative anticoagulants, evaluation of proton-pump inhibitor utilization, and other areas as identified and appropriate

Facility Responsibility

- Documentation and timely follow-up for clinically significant medication issues identified by dispensing and/or consultant pharmacists
- Access for consultant pharmacist to the facility EHR, including the eMAR. If such access is not feasible, discuss options with your consultant pharmacist
- Identification of a contact person to:
  - receive communication from consultant pharmacists regarding clinically significant medication issues via secured e-mail or other identified mechanism;
  - ensure time sensitive follow-up from prescribers for clinically significant recommendations, as per IMPACT Act requirements;
  - facilitate timely follow-up for other consultant pharmacist recommendations

NEW Generic Medications

- by Allen Lefkovitz

Generic Name	Brand Name	Date Generic Available
Budesonide 9 mg Tablet ER	Uceris® Tablet ER	7/20/18
Colesevelam 3.75 gram Powder for Oral Suspension	Welchol™ Powder	7/18/18
Clindamycin 1.2%/Benzoyl Peroxide 2.5% Topical Gel	Acanya® Topical Gel	7/6/18
Clindamycin 1% Topical Gel	Clindagel® Topical Gel	7/6/18
Luliconazole 1% Topical Cream	Luzu® Topical Cream	7/6/18

NEW Drug

Perseris™ Extended-Release Injectable Suspension

- by Dave Pregizer

Brand Name (Generic Name)	**Perseris [per SER is] (risperidone) [ris PER i done]**
How Supplied	90 mg and 120 mg extended-release injectable suspension supplied in single-dose kits containing a sterile syringe (labelled 'P') prefilled with risperidone powder, a sterile syringe (labelled 'L') prefilled with the delivery system and desiccant, and one 18-gauge, 5/8-inch sterile safety needle.
Therapeutic Class	Atypical antipsychotic
Approved Indication	Treatment of schizophrenia in adults
Usual Dosing	May be initiated at 90 mg or 120 mg subcutaneously in the abdomen monthly. Do not administer more than one dose per month or by any other route.
Select Drug Interactions	Strong CYP3A4 inducers (e.g., carbamazepine) decrease plasma concentrations of risperidone. Strong CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) increase risperidone plasma concentrations.
Most Common Side Effects	Increased weight, sedation/somnolence, and musculoskeletal pain.
Miscellaneous	Boxed warning for increased mortality in elderly patients with dementia-related psychosis. Establish tolerability with oral risperidone prior to use. Supplementation with oral risperidone is not recommended. Patients stable on oral risperidone doses less than 3 mg/day or more than 4 mg/day may not be candidates for Perseris.
Website	Perseris.com

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