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# Focus on Seasonal Influenza 2020-2021

by Allen Lefkovitz

A "twindemic", "a flu season wrapped in a global pandemic", and "a perfect storm" – each of these descriptions have been used by health officials to emphasize the importance of the influenza vaccine during the ongoing coronavirus disease 2019 (COVID-19) pandemic. As they have since 2010, the Advisory Committee on Immunization Practices (ACIP) continues to recommend routine annual influenza vaccination for everyone 6 months of age or older who do not have contraindications. Officials from the Centers for Disease Control and Prevention (CDC) describe influenza vaccination as "the most important thing we can do to help protect ourselves, our loved ones and our community from flu, including reducing the risk of serious outcomes that can lead to hospitalization and death." The 2020-2021 ACIP recommendations provide a few updates and many reminders, but ACIP stresses the importance of influenza vaccination "... to reduce prevalence of illness caused by influenza [that] will reduce symptoms that might be confused with those of COVID-19. Prevention of and reduction in the severity of influenza illness and reduction of outpatient illnesses, hospitalizations, and intensive care unit admissions through influenza vaccination also could alleviate stress on the U.S. health care system." Following a high severity 2017-2018 season and a prolonged 2018-2019 season, the importance of vaccinating for the 2020-2021 influenza season cannot be overstated.

### Influenza Vaccines for 2020-2021

The composition of the influenza vaccines for 2020-2021 is described described in the table, but represents a change in three of the four strains since last year's quadrivalent vaccines. This year CDC also recommended different compositions for egg-based versus non-egg-based vaccines, in order to account for different manufacturing processes while still providing the same overall protection.

| The 2020-2021 Egg-Based Quadrivalent Vaccines (A + A + B + B) |
|---|
| A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09-like virus |
| + |
| A/Hong Kong/2671/2019 (H3N2)-like virus |
| + |
| B/Washington/02/2019 (Victoria lineage)-like virus |
| + |
| B/Phuket/3073/2013 (Yamagata lineage)-like virus* |

* Strain not included in trivalent adjuvanted influenza vaccine

| The 2020-2021 Cell- or Recombinant-Based Quadrivalent Vaccines (A + A + B + B) |
|---|
| A/Hawaii/70/2019 (H1N1) pdm09-like virus |
| + |
| A/Hong Kong/45/2019 (H3N2)-like virus |
| + |
| B/Washington/02/2019 (Victoria lineage)-like virus |
| + |
| B/Phuket/3073/2013 (Yamagata lineage)-like virus |

CDC has worked with manufacturers to increase vaccine availability for the upcoming season, so while an overall shortage is not anticipated at this time, availability of specific formulations could be limited. Ten influenza vaccines are anticipated to be available for the 2020-2021 season, and are outlined in the table on page 2. All except for one product (Fluad) will be quadrivalent formulations. This season, two new influenza vaccines include Fluad Quadrivalent, and the Fluzone High-Dose

*Continued on next page*

**Table – Influenza Vaccines Available in 2020-2021**

| Trade Name | Manufacturer | Contains Mercury? | Approved Age Group |
|---|---|---|---|
| **Quadrivalent, Standard Dose, Inactivated Influenze Vaccine (SD-IIV4)** | | | |
| **Afluria Quadrivalent** | Seqirus | In MDV Only | ≥ 6 months* |
| **Fluarix Quadrivalent** | GlaxoSmithKline | No | ≥ 6 months |
| **FluLaval Quadrivalent** | GlaxoSmithKline | No | ≥ 6 months |
| **Fluzone Quadrivalent** | Sanofi Pasteur | In MDV Only | ≥ 6 months |
| **Quadrivalent, Standard Dose, Cell Culture-based Inactivated Influenza Vaccine (ccIIV4)** | | | |
| **Flucelvax Quadrivalent** | Seqirus | In MDV Only | ≥ 4 years |
| **Quadrivalent, High Dose, Inactivated Influenza Vaccine (HD-IIV4) **NEW for 2020-2021**** | | | |
| **Fluzone Quadrivalent High-Dose** | Saofi Pasteur | No | ≥ 65 years |
| **Quadrivalent, Recombinant Influenza Vaccine (RIV4)** | | | |
| **Flublock Quadrivalent** | Saofi Pasteur | No | ≥ 18 years |
| **Quadrivalent, Standard Dose, Inactivated Influenza Vaccine with Adjuvant (aIIV4) **NEW for 2020-2021**** | | | |
| **Fluad Quadrivalent** | Seqirus | No | ≥ 65 years |
| **Trivalent, Standard Dose, Inactivated Influenza Vaccine with Adjuvant (aIIV3)** | | | |
| **Fluad** | Seqirus | No | ≥ 65 years |
| **Intranasal, Quadrivalent, Live Attentuated Influenza Vaccine (LAIV4)** | | | |
| **FluMist Quadrivalent** | AstraZeneca | No | 2 to 49 years |

MDV: Multiple-dose vials

*Afluria Quadrivalent may also be given using a jet injector for those 18 to 64 years of age. A smaller 0.25 mL prefilled syringe is available for use only in children 6 to 35 months.

Quadrivalent, which was previously only available as a trivalent formulation. **An important difference to be aware of with Fluzone High-Dose Quadrivalent is that the volume administered in each injection is 0.7 mL intramuscularly, instead of the 0.5 mL dose used for all other injectable influenza vaccines.**

**Timing of Influenza Vaccine Administration**

ACIP recommends that "Optimally, vaccination should occur before onset of influenza activity in the community", and since it can take about 2 weeks to develop the necessary antibodies, they recommend vaccination "**by the end of October**." Because of COVID-19, many are suggesting vaccination efforts begin as soon as possible. However, routine vaccination should be deferred for individuals with suspected or confirmed COVID-19, regardless of symptoms until criteria have been met for them to discontinue isolation (e.g., no fever in the past 24 hours, improvement in symptoms; for more details see https://www.cdc.gov/vaccines/pandemic-guidance/index.html). CDC continues to encourage 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."

**Allergies and Influenza Vaccination**

CDC 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." CDC recommends that prescribers consider the prophylactic use of antiviral medications (e.g., oseltamivir) for individuals who are medically unable to receive influenza vaccination.

Except for recombinant influenza vaccine [(RIV4) i.e., Flublok Quadrivalent] and cell culture-based inactivated influenza vaccine [(ccIIV4) i.e., Flucelvax Quadrivalent], all influenza vaccines are made by growing viruses in embryonated chicken eggs and may contain small amounts of egg protein. ACIP recommends that anyone with a history of severe allergic reaction to eggs (i.e., more than hives) may receive any recommended and age appropriate influenza vaccine. However, if a vaccine other than Flublok Quadrivalent or Flucelvax Quadrivalent is to be administered to someone who has a more severe reaction to eggs (e.g., respiratory distress, swelling), the vaccine should be administered:

- in an inpatient or outpatient medical setting (including but not necessarily limited to hospitals, clinics, health departments, and physician offices); and
- only under the supervision of a healthcare provider who can 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.

**Influenza Vaccines and the Older Adult**

Unless otherwise medically contraindicated, being vaccinated is always preferable to not being vaccinated. But ACIP acknowledges that "The effectiveness of influenza vaccination varies depending upon several factors", including the recipient's health and age, the type of vaccine received, and the circulating influenza viruses. As they did last year, ACIP continues to note that "early vaccination (i.e., in July and August) is likely to be associated with suboptimal immunity before the end of the influenza season, particularly among older adults." This is because vaccine response may be reduced in older adults due to weakening of their immune system and overall frailty.

Since ACIP does not recommend the practice of revaccination (i.e., providing a booster dose) to anyone properly vaccinated, "active research" to help improve vaccine response and effectiveness for older adults has primarily revolved around three types of vaccines:

- Fluzone High-Dose Quadrivalent (HD-IIV4) - contains four times the amount of antigen compared to SD-IIV4
- Flublok Quadrivalent (RIV4) – recombinant vaccine that contains three times the antigen compared to SD-IIV4
- Fluad (aIIV3) and Fluad Quadrivalent (aIIV4) – contain an adjuvant that enhances the body's response to the vaccine but is the least studied of these options

The expert recommendation of ACIP is that "For Persons aged ≥ 65 years, any age-appropriate IIV [inactivated influenza vaccine] formulation (standard dose or high dose, trivalent or quadrivalent, nonadjuvanted or adjuvanted) or RIV4 is an acceptable option." However, clinical evidence in older adults increasingly supports additional consideration of using Fluzone High-Dose Quadrivalent, Flublok Quadrivalent, or either adjuvanted Fluad formulation instead of standard-dose formulation.

**Influenza Vaccination and Long-Term Care**

Nursing Home Compare data currently indicate that 96% of long-stay residents and 82.9% of short-stay residents who "needed" an influenza vaccine received it. ACIP continues to classify all residents of nursing homes and other long-term care facilities (LTCF) as being at "higher risk for influenza-related complications". In support of CDC recommendations, the Centers for Medicare and Medicaid Services (CMS) states "Facilities should administer the influenza vaccine when it becomes available to the facility." Within F883 "Influenza and pneumococcal immunizations", CMS 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 (without any guidance related to vaccine type) 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.

Extra attention must also be given to those who have direct contact with long-term care residents. ACIP states this may include (but not be limited to) "physicians, nurses, nursing assistants, nurse practitioners, physician assistants, therapists, technicians, emergency medical service personnel, dental personnel, pharmacists, laboratory personnel, autopsy personnel, students and trainees, contractual staff, and other persons not directly involved in patient care but who can potentially be exposed to infectious agents (e.g., clerical, dietary, housekeeping, laundry, security, maintenance, administrative, billing, and volunteers)." CDC recognizes that "Influenza vaccination among health care personnel in long-term care settings is especially important because influenza vaccine efficacy is generally lowest among the elderly, who are at increased risk for severe disease". Unfortunately, the most recent information from the 2018-2019 season continues to indicate that LTCF remain the segment of healthcare with the lowest vaccination rate among healthcare professionals at 67.9% (compared to an overall average of 81.1%). As a result, CDC strongly encourages efforts to improve vaccination coverage in LTCF, especially among staff.

**Average Rate of Vaccination Among Healthcare Professionals**

**81.1%**
All Healthcare Professionals

**67.9%**
Long-Term Care Healthcare Professionals

To prepare for the upcoming and unpredictable influenza season, please refer to the summary of the ACIP recommendations and other helpful influenza resources available at: www.cdc.gov/flu/.

# Antiviral Agents Used for Influenza Treatment and Prevention

by Allen Lefkovitz and Palak Patel

According to the Centers for Disease Control and Prevention (CDC), use of antiviral agents "is a key component of influenza outbreak control". CDC states that "All long-term care facility residents who have confirmed or suspected influenza should receive antiviral treatment immediately" and "All exposed residents on units or wards with influenza cases in the long-term care facility (currently impacted wards) should receive antiviral chemoprophylaxis as soon as an influenza outbreak is determined." An overview of FDA recommended dosing for the three neuraminidase inhibitors and the first-in-class polymerase acidic endonuclease inhibitor is provided below. Older antiviral medications (i.e., amantadine and rimantadine) are not recommended for use. 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 to 60 mL/min** | 30 mg twice daily for 5 days | 30 mg once daily for **at least 14 days** |
| **CrCl > 10 to 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 every dialysis cycle for 5 days | 30 mg immediately and then 30 mg 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 and then 30 mg once weekly 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 x 1 dose |
| **CrCl = 30 to 49 mL/min** | 200 mg x 1 dose |
| **CrCl = 10 to 29 mL/min** | 100 mg x 1 dose |
| **ESRD on Hemodialysis** | After dialysis at a dose based on renal function |

**Xofluza (baloxavir) Tablet¶‖**

| Weight | Treatment Dose for Adults |
|---|---|
| **40 kg to less than 80 kg** | Single dose of 40 mg |
| **At least 80 kg** | Single dose of 80 mg |

CrCl = creatinine clearance; ESRD = end stage renal disease; FDA = the U.S. Food and Drug Administration; LTC = long-term care

* According to the CDC, within LTC facilities, the recommended minimum length of therapy for prophylaxis is "a minimum of 2 weeks, and continuing for at least 7 days after the last known laboratory-confirmed influenza case was identified on affected units".
† No dosage adjustment is necessary in those with renal impairment, but 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.
¶‖ Not FDA approved for prophylaxis. Use in those with a CrCl below 50 mL/min has not been fully evaluated.

# NEW Generic Medications

by Allen Lefkovitz

| Generic Name | Brand Name | Date Generic Available |
|---|---|---|
| **Efavirenz/Lamivudine/Tenofovir 600 mg/300 mg/300 mg Tablet** | Symfi® Tablet | 9/3/20 |
| **Efavirenz/Lamivudine/Tenofovir 400 mg/300 mg/300 mg Tablet** | Symfi Lo® Tablet | 9/3/20 |
| **Nitisinone 2 mg, 5 mg, and 10 mg Capsule** | Orfadin® Capsule | 9/3/20 |
| **PEG-3350, Sodium Sulfate, Sodium Chloride, Potassium Chloride, Sodium Ascorbate, and Ascorbic Acid Powder for Oral Solution** | MoviPrep® Powder | 9/3/20 |
| **Emtricitabine 200 mg Capsule** | Emtriva® Capsule | 9/3/20 |
| **Dimethyl Fumarate 120 mg and 240 mg Capsule** | Tecfidera® DR Capsule | 8/20/20 |
| **Pantoprazole 40 mg DR Granules for Suspension** | Protonix® Packets for DR Suspension | 8/17/20 |
| **Deferasirox 90 mg, 180 mg, and 360 mg Granules** | Jadenu® Sprinkle | 8/14 to 8/24/20 |
| **Ciprofloxacin/Dexamethasone 0.3%/0.1% Otic Suspension** | Ciprodex® Otic Suspension | 8/13/20 |
| **Imiquimod* 3.75% Cream** | Zyclara® Cream | 8/7/20 |
| **Metyrosine 250 mg Capsule** | Demser® Capsule | 8/3/20 |
| **Desonide 0.05% Gel** | Desonate® Gel | 7/10/20 |

* Not an A-rated generic; substitution policies may vary by state and how orders are written

# NEW Drugs

by Dave Pregizer

## Breztri Aerosphere™

| Brand Name (Generic Name) | Breztri Aerosphere™ [brez-TREE] (budesonide-glycopyrrolate-formoterol fumarate) |
|---|---|
| **How Supplied** | Pressurized metered dose inhaler with 28 or 120 inhalations, containing budesonide (160 mcg), glycopyrrolate (9 mcg), and formoterol fumarate (4.8 mcg) per inhalation |
| **Therapeutic Class** | Combination of a corticosteroid, anticholinergic, and long-acting beta2-adrenergic agonist |
| **Approved Indication** | Maintenance treatment of patients with chronic obstructive pulmonary disease |
| **Usual Dosing** | Two oral inhalations twice daily. Rinse mouth with water without swallowing after each use. |
| **Select Drug Interactions** | Strong cytochrome P450 3A4 inhibitors (e.g., clarithromycin) may increase exposure to budesonide. Diuretics, xanthine derivatives or steroids may potentiate hypokalemia or ECG changes. MAO inhibitors and tricyclic antidepressants may potentiate effect of formoterol on cardiovascular system. Beta-blockers may produce severe bronchospasm. |
| **Most Common Side Effects** | Upper respiratory tract infection, pneumonia, back pain, oral candidiasis, influenza, muscle spasm, urinary tract infection, cough, sinusitis, and diarrhea |
| **Miscellaneous** | Not for acute bronchospasm or treatment of asthma. Severe hepatic impairment may increase systemic exposure of budesonide and formoterol. |
| **Website** | http://www.Breztri.com |