Update—Influenza Vaccination and Antiviral Recommendations

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IHS Call
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Overview

- Update on 2015-16 ACIP influenza vaccination recommendations

- Very brief overview of indications for antiviral treatment for influenza
2015-16 ACIP Influenza Vaccination Statement


- Annual influenza vaccination is recommended for all persons aged 6 months and older

- Topics discussed:
  - Influenza vaccine virus composition for 2015-16
  - New FDA-approvals since the 2014-15 statement
  - Update in dosing algorithm for children aged 6 mos. through 8 yrs.
  - Updated recommendations regarding use of LAIV and IIV for healthy 2 through 8 year olds, including removal of LAIV preference

- For topics not addressed, refer to 2013-14 statement
Vaccine Composition for 2015-16

Two strain changes compared with the 2014-15:

- For trivalent vaccines,
  - an A/California/7/2009 (H1N1)pdm09-like virus (same as 2014-15);
  - An A/Switzerland/9715293/2013 (H3N2)-like virus (replaces A/Texas/50/2012 (H3N2)-like)
  - A B/Phuket/3073/2013-like virus (Yamagata lineage; replaces previous B/Massachusetts/2/2012-like Yamagata lineage virus)

- For quadrivalent vaccines,
  - The above three viruses and a B/Brisbane/60/2008-like virus (Victoria lineage; same as 2014-15)
# Licensed Seasonal Influenza Vaccines, United States, 2015-16 Season

**TABLE. Influenza vaccines — United States, 2015–16 influenza season**

<table>
<thead>
<tr>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Presentation</th>
<th>Mercury (from thimerosal) μg/0.5 mL</th>
<th>Ovalbumin μg/0.5 mL</th>
<th>Age indications</th>
<th>Latex</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactivated influenza vaccine, quadrivalent (IV4), standard dose</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>FluVarix Quadrival</td>
<td>GlaxoSmithKline</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>—</td>
<td>≤0.05</td>
<td>≥3 yrs</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td>FluLaval Quadrival</td>
<td>ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)</td>
<td>5.0 mL multi-dose vial</td>
<td>&lt;25</td>
<td>≤0.3</td>
<td>≥3 yrs</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td>FluZone Quadrival</td>
<td>Sanofi Pasteur</td>
<td>0.25 mL single-dose prefilled syringe</td>
<td>—</td>
<td>5</td>
<td>6 through 35 mos</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td>FluZone IntradermalQuadrival</td>
<td>Sanofi Pasteur</td>
<td>0.1 mL single-dose prefilled syringe</td>
<td>25</td>
<td>5</td>
<td>6 through 64 yrs</td>
<td>No</td>
<td>ID**</td>
</tr>
<tr>
<td><strong>Inactivated influenza vaccine, trivalent (IV3), standard dose</strong></td>
<td></td>
<td></td>
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<tr>
<td>Affluria</td>
<td>bioCSL</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>24.5</td>
<td>&lt;1</td>
<td>≥9 yrs††</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multi-dose vial</td>
<td>24.5</td>
<td>&lt;1</td>
<td>≥9 yrs†† via needle; 18 through 64 yrs via jet injector</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td>Fluvirin</td>
<td>Novartis Vaccines and Diagnostics</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≤1</td>
<td>≤1</td>
<td>≥4 yrs</td>
<td>Yes§§</td>
<td>IM†</td>
</tr>
<tr>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>25</td>
<td>≤1</td>
<td>≥4 yrs</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multi-dose vial</td>
<td>25</td>
<td>≤1</td>
<td>≥6 mos</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td><strong>Inactivated influenza vaccine, cell-culture-based (ccIV3), standard dose</strong></td>
<td></td>
<td></td>
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<tr>
<td>FluCell</td>
<td>Novartis Vaccines and Diagnostics</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>—</td>
<td>≥18 yrs</td>
<td>Yes§§</td>
<td>IM†</td>
<td></td>
</tr>
<tr>
<td><strong>Inactivated influenza vaccine, trivalent (IV3), high dose</strong></td>
<td></td>
<td></td>
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<tr>
<td>FluZone High-Dose***</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>—</td>
<td>5</td>
<td>≥65 yrs</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td><strong>Recombinant influenza vaccine, trivalent (RV3), standard dose</strong></td>
<td></td>
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<tr>
<td>FluBlok</td>
<td>Protein Sciences</td>
<td>0.5 mL single-dose vial</td>
<td>—</td>
<td>0</td>
<td>≥18 yrs</td>
<td>No</td>
<td>IM†</td>
</tr>
<tr>
<td><strong>Live attenuated influenza vaccine, quadrivalent (LAI4)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>FluVarix Quadrival</td>
<td>MedImmune</td>
<td>0.2 mL single-dose prefilled intranasal sprayer</td>
<td>—</td>
<td>&lt;0.24 (per 0.2 mL)</td>
<td>2 through 49 yrs</td>
<td>No</td>
<td>IN</td>
</tr>
</tbody>
</table>

See table footnotes on page next page.

MMWR (2015) 64;30: 818-825
Influenza Vaccine Product Updates for 2015-16

New licensures, labeling information, and other changes:

- **Fluzone® Intradermal Quadrivalent IIV**
  - Replaces previous trivalent formulation of Fluzone Intradermal
  - Non-inferior immunogenicity, similar adverse event profile to trivalent

- **Expanded age indication for Flublok® (now 18 and older)**
  - Previously licensed for 18 through 49 years
  - Similar immunogenicity and safety among persons 50 years and over

- **Approval of administration of Afluria® by Stratis® jet injector**
  - for persons 18 through 64 years of age
  - Ages 9 through 17 years, 65 years and over—needle/syringe only
  - ACIP does not recommend Afluria under 9 years
  - No other influenza vaccines currently licensed for use with a jet injector

- **Some presentation changes**
  - Flulaval and Fluarix trivalents no longer available (quadrivalents only)
  - Fluzone standard dose trivalent still available, but only multidose vial
    (quadrivalent available in all four presentations)

MMWR (2015) 64;30: 618-625
Available Influenza Vaccine Products, 2015-16
General Characteristics

- Live virus vs. not
- Trivalent vs. quadrivalent
- Standard-dose vs. high-dose
- Egg-based vs. non-egg based
- Intramuscular vs. intradermal vs. intranasal
Currently Available Influenza Vaccines (N=11)
Common Features

- Contain hemagglutinin (HA) derived from
  - an Influenza A(H1N1) virus,
  - an Influenza A(H3N2) virus, and
  - One (if trivalent) or two (if quadrivalent) Influenza B viruses
Available Influenza Vaccine Products, 2015-16
(11 Branded Products)

- **9 inactivated vaccine products (IIVs)**
  - 4 quadrivalent
    - All standard dose, all egg-based
    - 3 intramuscular, 1 intradermal
  - 3 trivalent, standard dose, egg-based (IIV3)—intramuscular
  - 1 trivalent, standard dose, cell culture-based (ccIIV3)—intramuscular
  - 1 trivalent, high dose, egg based (high dose IIV3)—intramuscular

- **1 live attenuated vaccine product (LAIV)**
  - Quadrivalent only (LAIV4)—intranasal

- **1 recombinant vaccine product (RIV)**
  - Trivalent only (RIV3)—intramuscular
Trivalent Inactivated Influenza Vaccines (IIV3s)

- Have different age indications; need to check package insert
  - An age-appropriate product should be used
  - Products available for persons as young as 6 months
- All are egg-based EXCEPT Flucelvax® (Novartis)—MDCK cells
- All contain 15µg of HA per virus EXCEPT Fluzone® High-Dose
  - Contains 60µg HA per virus
  - Approved for persons aged 65 years and older
  - 24.2% more effective than standard dose IIV3 in preventing lab confirmed influenza among persons 65 and older in one RCT
- All are administered intramuscularly (needle/syringe)
- One (Afluria®, bioCSL) approved for administration via jet injector
  - *May be administered by sterile needle and syringe (ages 9 and older),*
  - *OR by Stratis® (PharmaJet) jet injector (ages 18 through 64 years ONLY)*
Quadrivalent Inactivated Influenza Vaccines (IIV4s)

- **Provide broader protection against Influenza B viruses**
  - There are two Influenza B lineages: Victoria and Yamagata
  - Immunization against virus from one lineage provides only limited cross-protection against viruses in the other
  - Predominant lineage difficult to predict ahead of each season
  - *Trivalent vaccines contain only one B vaccine virus*
  - *Quadrivalents contain two B viruses (one from each lineage)*

- **All contain 15µg of HA per virus EXCEPT Fluzone® Intradermal Quadrivalent**

- **All are administered intramuscularly EXCEPT Fluzone Intradermal Quadrivalent (intradermal)**
  - *Administered with device included in packaging*
  - *9 mcg per HA virus*

- **Three different products; one approved for as young as 6 mos**
Vaccines Produced via Non-Egg-Based Technologies

- May permit more rapid scale up of vaccine production (e.g., as might be needed during a pandemic)

- Two vaccines this season, both only trivalents currently:
  - Cell culture-based
  - Recombinant HA
Cell Culture-Based Inactivated Influenza Vaccine (ccIIV3)

- Flucelvax® (Novartis)
- Approved for persons aged 18 and older
- Licensed in the U.S. in 2012; in the EU since 2007
- Currently available only in a trivalent formulation
- Vaccine viruses propagated in Madin-Darby Canine Kidney cells rather than in eggs
- However, initial reference strains are passaged in eggs
  - Cannot be considered egg-free in the U.S.
  - Per mfr, estimated to be <50 femtograms (5x10^{-8} µg) per 0.5mL dose
- For egg allergic persons, ACIP recs treat ccIIV same as egg-based IIVs
Recombinant Influenza Vaccine (RIV3)

- **FluBlok® (Protein Sciences)**
- Approved for persons aged 18 years and over
- Currently available only in trivalent formulation
- Considered egg-free
- **Vaccine contains recombinant influenza virus HA**
  - HA produced via introduction of the gene sequence into an insect cell line (Fall Armyworm) using a baculovirus vector
  - Contains 45 mcg HA derived from each vaccine virus (135 mcg total)
- **Per ACIP recs, is an option for persons with egg allergy of any severity (for those within the indicated age range)**
Live Attenuated Influenza Vaccine (LAIV4)

- FluMist® (MedImmune)
- Administered intranasally
- Quadrivalent only since 2013-14
- Approved for persons aged 2 through 49 years
  - ACIP recommends only for certain populations
Currently Available Influenza Vaccines (N=11)

- For many people, more than one option—examples:
  - Healthy 2 through 49 year olds—LAIV or IIV?
  - 65 years and older—standard dose or high dose IIV?
  - Pretty much anyone—quadrivalent or trivalent?

- ACIP makes no preferential recommendations for one product over another in situations where more than one is appropriate for a given individual
Determining Doses Needed for Children 6 months through 8 Years of Age

• Since 2010, counted doses of A(H1N1)pdm09 (2009 pandemic virus) separately
• For 2015-16, not counting separately doses of vaccine containing A(H1N1)pdm09
• If child in this age group has received ≥2 doses trivalent or quadrivalent influenza vaccine before July 2015, needs only one dose of 2015-16 vaccine
  • The 2 doses do not need to be from same or consecutive seasons)

FIGURE 1. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season

Has the child received ≥2 total doses of trivalent or quadrivalent influenza vaccine before July 1, 2015*

Yes

1 dose of 2015–16 influenza vaccine

No or don't know

2 doses† of 2015–16 influenza vaccine

* The two doses need not have been received during the same season or consecutive seasons.
† Doses should be administered ≥4 weeks apart.

MMWR (2015) 64;30: 618-625
Persons for Whom LAIV Should Not Be Used (1)

LAIV should not be used in the following populations:

- Persons aged <2 years or >49 years;
- Those with contraindications listed in the package insert:
  - Children and adolescents receiving aspirin or aspirin-containing products;
  - Persons who have experienced severe allergic reactions to the vaccine or any of its components, or to a previous dose of any influenza vaccine;
- Pregnant women;
- Immunosuppressed persons;
- Persons with a history of egg allergy;
- Children aged 2 through 4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health care provider stated that they had wheezing or asthma within the last 12 months;
Persons for Whom LAIV Should Not Be Used (2)

In addition to those on the previous slide, LAIV should not be used in the following populations (continued):

- Persons who have taken influenza antiviral medications within the previous 48 hours.

- Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV, or should avoid contact with such persons for 7 days after receipt.
Precautions for the Use of LAIV

In addition to groups for whom LAIV is not recommended, the following are precautions for use of LAIV:

- Medical conditions that predispose to high risk of complications due to influenza (labeled precaution per the package insert);
- Asthma in persons aged ≥5 years (package insert notes potential increased risk of wheezing).
- Guillain-Barré Syndrome within 6 weeks of a prior dose of influenza vaccine (a precaution for all influenza vaccines)
- Moderate to severe illness with or without fever (a precaution for all influenza vaccines)
Influenza Antiviral Drugs: 2015-16

- **Neuraminidase inhibitors (NAIs): oseltamivir (Tamiflu), zanamivir (Relenza), peramivir (Rapivab)**
  - For treatment and prevention of influenza A and B
  - >99% of all circulating viruses were susceptible to NAIs during 2014-15
  - *Are recommended* for use during this season

- **Investigational drug available: IV zanamivir**

- **Adamantanes: rimantadine and amantadine**
  - High levels of resistance
  - *Not recommended* for use during this season
CDC Antiviral Recommendations

- All patients in the following categories with suspected or confirmed influenza should be treated as soon as possible, without waiting for confirmatory influenza testing

  - Hospitalized patients
  
  - Patients with severe, complicated, or progressive illness
  
  - Patients at high risk for complications from influenza (either outpatient or hospitalized)
CDC Antiviral Recommendations

- Antiviral treatment **may** be prescribed on the basis of clinical judgment for any previously healthy (non-high risk) outpatient with suspected or confirmed influenza.
Persons at High Risk for Influenza Complications

- Children <2 years
- Adults >65 years
- Pregnant and postpartum (2 weeks after delivery)
- American Indians and Alaska Natives
- Persons who are morbidly obese (BMI >40)
- Residents of long-term care facilities
Persons at High Risk for Influenza Complications (continued)

- Persons with immunosuppression
- Persons <19 years who are receiving long-term aspirin therapy
- Persons with underlying medical conditions: chronic pulmonary, cardiovascular (except hypertension alone), renal, hepatic, hematologic, and metabolic disorders (incl. diabetes), or neurologic and neurodevelopment conditions
Influenza Antiviral Medications: The Data Behind the Recommendations

Clinical trials and observational data show that early antiviral treatment can:

- Shorten the duration of fever and illness symptoms
- Reduce the risk of complications (such as otitis media in children and pneumonia requiring antibiotics in adults)
- Reduce the risk of death among hospitalized patients
Efficacy of Neuraminidase Inhibitors: Uncomplicated influenza

Uncomplicated influenza (ambulatory patients)

- Reduces duration of influenza symptoms by average of 1-1.5 days when administered within 2 days of illness onset based on randomized placebo-controlled clinical trials (RCTs)
  - Reduces shedding by 20-30% each day, compared to placebo
  - Persons treated develop immunity
Thank You!

For more information please contact Centers for Disease Control and Prevention

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Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
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