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Influenza Vaccine 2010-2011 Update

By Marcia Wyman, Pharm.D.

Introduction: Annual vaccination against influenza A and B viruses is the most effective way to prevent influenza and its related complications.[1] Influenza epidemics usually occur during the late fall through early spring in the United States. Seasonal influenza vaccines are typically available in early fall, while their antigenic components are determined the prior spring. An unexpected appearance of the H1N1 virus producing the first pandemic since 1968 occurred during spring 2009. Since the 2009-2010 seasonal influenza vaccine was already formulated, a monovalent vaccine specifically designed to protect against the H1N1 virus was developed. Consequently, patients needed to receive both the seasonal and H1N1 vaccines to acquire full protection against influenza viruses during the 2009-2010 influenza season. Scientists believe that the H1N1 virus will persist during future winter influenza seasons necessitating the addition of the H1N1 viral antigen into the 2010-2011 influenza vaccines as well as some changes in recommendations by the Advisory Committee on Immunization Practices (ACIP).[1]

Different Antigenic Components: The seasonal influenza vaccine for 2010-11 contains these antigens:

- A/California/7/2009(H1N1)-like
- A/Perth/16/2009(H3N2)-like
- B/Brisbane/60/2008-like

The H1N1 antigen is the same one previously incorporated into the H1N1 2009 monovalent influenza vaccine.[1-3] Therefore, the new influenza formulation alleviates the need for a separate H1N1 vaccine this year. Approximately 160-165 million doses of influenza vaccine should be available for the 2010-2011 influenza season from six different manufacturers.[4]

Larger Target Population: As of February 24, 2010, the ACIP broadened its recommendation for seasonal influenza vaccine to encompass not only certain high-risk groups but all individuals 6 months and older unless otherwise contraindicated.[1-3] The expansion of the target population is based on concerns that the H1N1 virus which is associated with an increased risk of influenza-induced complications in adults 19-49 years of age will continue to circulate throughout the 2010-2011 influenza season.[1]

New High-Dose Vaccine: Fluzone® High-Dose is a new vaccine formulation which is approved by the Food and Drug Administration for patients 65 years and older.[1-3] It is an inactivated vaccine which contains approximately four times the amount of antigen as the regular strength Fluzone® (60 mcg versus 15 mcg of hemagglutinin antigen, respectively).

This higher strength vaccine was designed to provide greater protection against influenza for elderly patients who typically have a diminished immune response to vaccines compared to healthy young adults.[1] Compared with regular strength Fluzone®, Fluzone® High-Dose has been shown to produce higher antibody levels in healthy individuals 65 years and older. However, clinical studies have not correlated these higher antibody levels with greater clinical efficacy.[2] Furthermore, Fluzone® High-Dose has been shown to cause more injection site reactions producing more arm pain, redness, and swelling than the regular strength formulation.[2,3] Therefore, the ACIP states that patients 65 years or older may receive either the standard or high-dose inactivated influenza vaccine; those under the age of 65 years should receive the standard formulation.[1]

Updated Pediatric Dosage Recommendations: The ACIP recommends that children 6 months through 8 years of age receive two doses of the 2010-2011 seasonal vaccine spaced 4 weeks apart under these circumstances:

1) First-time vaccination;
2) No previous vaccine history;
3) Previously received only one dose of the seasonal 2009-2010 influenza vaccine; or
4) No record of receiving at least one dose of H1N1 2009 vaccine regardless of previous influenza vaccine history

Vaccine Availability: Cleveland Clinic Health System will carry the following brands of seasonal 2010-2011 vaccine:

- FluLaval®
- Fluarix®
- Fluzone®
- Fluzone® High-Dose
- FluMist®

Various characteristics of these vaccine formulations such as latex and thimerosal content are summarized in Table 1.

Storage and Stability: It is generally recommended that the seasonal 2010-2011 influenza vaccine preparations be stored under refrigeration at 2° to 8°C (36° to 46°F) and should not be frozen.[5-8] However some circumstances (e.g., refrigerator malfunction) may expose the vaccines to deviations from the recommended temperature range which may affect product stability and/or sterility. Information about recommended storage conditions and product stability at various temperature ranges is provided in Table 2.

Conclusion: Last year's H1N1 influenza pandemic prompted some important alterations in ACIP recommendations. The 2010-2011 seasonal influenza vaccine which contains the H1N1 antigen is recommended for all individuals 6 months and older unless otherwise contraindicated. A new high-dose influenza formulation is available to help boost immune response in individuals 65 years and older. Pediatric patients who did not receive at least one dose of the H1N1 monovalent vaccine in 2009, should receive two doses of the 2010-2011 seasonal influenza vaccine regardless of their previous vaccine history. Various ACIP recommendations along with other related information can be found on the Centers for Disease Control and Prevention influenza website (http://www.cdc.gov/flu).

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Influenza Vaccine 2010-2011

Table 1: Characteristics of Select Influenza Vaccine Preparations[5-8]

Brand Name	Manufacturer	Presentation	Indication	Inactivated (I) or Live (L)	Latex (Y/N)	Egg Protein (Y/N)	Thimerosal (Y/N)	Gentamicin (Y/N)
FluLaval®	GSK*	5 mL (multi-dose vial)	18 years and older	I	N	Y	Y	N
Fluarix®	GSK*	0.5 mL (PFS†)	36 months to adult	I	Y	Y	N	Y
Fluzone®	Sanofi Pasteur	5 mL (multi-dose vial)	6 months to adult	I	N	Y	Y	N
Fluzone®	Sanofi Pasteur	0.5 mL (PFS†)	36 months to adult	I	Y	Y	N	N
Fluzone®	Sanofi Pasteur	0.25 mL (Pediatric PFS†)	6 to 35 months	I	Y	Y	N	N
Fluzone®	Sanofi Pasteur	0.5 mL (**High-Dose** PFS†)	65 years and older	I	Y	Y	N	N
FluMist®	MedImmune	0.5 mL Nasal (Single-Use Sprayers)	Non-pregnant 2 to 49 years	L	N	Y	N	Y

*GSK= GlaxoSmithKline
†PFS=prefilled syringe
FluLaval®, Fluarix®, and Fluzone® may contain trace amounts of formaldehyde
FluMist® contains porcine-derived gelatin and monosodium glutamate
Fluzone® multi-dose vial and PFS contain porcine-derived gelatin; Fluzone® High-Dose does not contain porcine-derived gelatin
Note: The information in Table 1 only applies to the 2010-2011 influenza vaccine and may change annually.

Influenza Vaccine 2010–2011

Table 2: Storage Recommendations for Select Influenza Vaccine Preparations[5-12]

Brand Name	Presentation	Package Insert (Recommended Storage Conditions)	Stability Information for Exposure to ABOVE Recommended Temperature Range	Stability Information for Exposure to BELOW Recommended Temperature Range
FluLaval®	5 mL (multi-dose vial*)	2° to 8°C (36° to 46°F); Do NOT freeze; Discard if vaccine has been frozen; Store in the original package to protect from light; Do not use after expiration date shown on label	8° to 25°C (46° to 77°F); Stable for 72 **cumulative** hours‡	0° to 2°C (32° to 36°F); No stability data available; Discard if frozen
Fluarix®	0.5 mL (PFS†)	2° to 8°C (36° to 46°F); Do NOT freeze; Discard if vaccine has been frozen; Store in the original package to protect from light; Do not use after expiration date shown on label	8° to 25°C (46° to 77°F); Stable for 72 **cumulative** hours	0°to 2°C (32°to 36°F); No stability data available; Discard if frozen
Fluzone®	5 mL (multi-dose vial*)	2° to 8° C (35° to 46° F); Do NOT freeze; Discard if vaccine has been frozen; Between uses, return multi-dose vial to recommended temperature range; Do not use after expiration date shown on label	Stable for 30 minutes at temperatures up to 77°F; for other excursions need to call manufacturer with specific temperature range and time of exposure Sanofi Pasteur 1-800-822-2463	Need to call manufacturer with specific temperature range and time of exposure; Discard if frozen Sanofi Pasteur 1-800-822-2463
Fluzone®	0.5 mL (PFS†)			
Fluzone®	0.25 mL (Pediatric PFS†)			
Fluzone®	0.5 mL (**High-Dose** PFS†)			
FluMist®	0.5 mL Nasal (Single-Use Sprayers)	2 to 8°C (35 to 46°F); Do NOT freeze; The product must be used before the expiration date on the sprayer label	8° to 15°C (46° to 59°F); Place back in refrigerator and use within 48 hours of exposure >15° to 25°C (>59° to 77°F); Keep at room temperature and use within 12 hours of exposure	If accidental freezing occurs, avoid further exposure to freezing conditions and use vaccine as soon as possible; may be placed back in refrigerator temperature range

**The Centers for Disease Control and Prevention (CDC) does not recommend prefilling plastic syringes with individual doses of influenza vaccine from multiple-dose vials due to lack of stability data; however a healthcare worker may draw up a small quantity of vaccine to meet the initial needs of an influenza clinic. All remaining vaccine in prefilled plastic syringes must be discarded at the end of the clinic day.*

***Note** Prefilled plastic syringes of FluLaval® and Fluzone® should be stored in a refrigerator or cooler and MUST be used the same day of preparation or be discarded.*

†PFS=prefilled syringe

‡Cumulative hours = total number of hours (cumulative hours do not have to be consecutive)

Note: The information in Table 2 only applies to the 2010-2011 influenza vaccine and may change annually.

Formulary Update

There is now a Medical Staff P&T Committee that is responsible for making formulary decisions for the entire Cleveland Clinic Health System (CCHS). The Committee's first meeting was in May 2010. The main campus will still have a Cleveland Clinic Local P&T Committee to determine if any further restrictions are needed on these formulary decisions as well as handle any medication-related issues that are specific to the main campus, FHCs, and ASCs. The Cleveland Clinic Local P&T Committee met on June 1, 2010, and the following decisions were made:

Formulary Additions/Changes:

1. **Abelcet® is the CCHS Formulary lipid amphotericin B product:** Abelcet® is already the Formulary restricted lipid amphotericin B product for both adults and pediatrics; therefore, there is no change in product for the Main Campus.
2. **Nafcillin is the CCHS Formulary antistaphylococcal penicillin:** We are using oxacillin currently; therefore, this will be a change for the Main Campus (Effective, July 13, 2010).
3. **Collagenase clostridium (Xiaflex®):** It is FDA-approved for the treatment of Dupuytren's contracture (DC) with palpable cord. The current standard of care of DC is open fasciectomy, percutaneous fasciotomy or needle fasciotomy. Surgery is recommended in patients with functional impairment of the metacarpophalangeal (MCP)-joint contractures of 30 degrees or more. Serious adverse events with the use of Xiaflex® include tendon rupture (2 patients), complex regional pain syndrome (1 patient), ligament disrupture (1 patient), and flexor pulley rupture (1 patient). The Food and Drug Administration (FDA) required a Risk Evaluation and Mitigation Strategy (REMS) for Xiaflex®, which involves distribution of a medication guide, physicians must complete a training program prior to using the medication, and pharmacies must register to receive the medication. Injections of Xiaflex® may be administered up to 3 times per cord at approximately 4 week intervals. The cost of a single dose for one joint is $3250 (for 2 doses for one joint, the cost is $6500 and for 3 doses for one joint, the cost is $9750). Its use is **restricted** to hand surgeons in the hospital outpatient setting for adult patients (and insurance coverage should be verified prior to administering the medication).
4. **Tocilizumab (Actemra®):** It is FDA-approved for the treatment of adult patients with moderately-to-severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. It may be used alone or in combination with methotrexate or other disease-modifying antirheumatic drugs (DMARDs). Tocilizumab is a recombinant humanized interleukin-6 receptor-inhibiting monoclonal antibody. Interleukin-6 is a proinflammatory cytokine commonly expressed in patients with rheumatoid arthritis and detectable in the joints and circulation during active phases of the disease. The most common adverse events reported in clinical trials included upper respiratory tract infections, nasopharyngitis, headache, hypertension, and increased ALT. Infusion reactions have included transient increase in blood pressure, injection-site redness, headache, nausea, skin eruptions, vomiting, pruritus, and malaise. Increases in total cholesterol, high-density lipoprotein cholesterol, and triglycerides were also observed during tocilizumab therapy. Patients should be monitored for clinical response and for signs and symptoms of infection. All patients should be screened for latent TB infection prior to starting tocilizumab. Neutrophils, platelets, and ALT and AST should be monitored every 4 to 8 weeks. Lipid parameters should be assessed approximately 4 to 8 weeks after initiation of therapy and then at approximately 6-month intervals. Tocilizumab is administered as an IV infusion every 4 weeks. It is infused over 1 hour. The recommended starting dose of tocilizumab when used as monotherapy or in combination with a DMARD is 4 mg/kg IV, followed by an increase to 8 mg/kg based on clinical response. Doses of more than 800 mg per infusion are not recommended. Its use is restricted to adult patients with rheumatoid arthritis in the hospital outpatient setting.

Formulary Denial:

Telavancin (Vibativ™): It is a new lipoglycopeptide antimicrobial with a structure and spectrum of activity similar to vancomycin. This agent has coverage against methicillin-susceptible and -resistant staphylococci as well as streptococci species. While it has activity against vancomycin-susceptible enterococci, it has no activity against vancomycin-resistant enterococci (VRE). Telavancin should not be used in pregnant women and will have a REMS associated with it to prevent unintended consequences in pregnant women. Telavancin was associated with nephrotoxcity in clinical trials when compared to vancomycin-treated patients. Also, clinical cure rates were lower in telavancin-treated patients with CrCl <50 ml/min compared to those with CrCl >50 ml/min. In addition, QTc prolongation has been noted, therefore, telavancin should be used with caution when given with other agents that may prolong QTc. Telavancin interferes with PT/INR, aPTT, activated clotting time and coagulation based factor Xa tests for up to 18 hours after administration. In summary, telavancin has limited (if any) added benefit over our current Formulary agents.