

# Influenza Vaccine (Seasonal)

## (Systemic)

Inactivated virus vaccine. Seasonal influenza virus vaccine inactivated is a trivalent vaccine containing noninfectious, suitably inactivated influenza virus types A and B subunits and is used to stimulate active immunity to influenza virus strains contained in the vaccine.

**Class:** Vaccines 80:12 (AHFS primary); im100 (VA primary)

**Brands:** Afluria<sup>®</sup>; Fluarix<sup>®</sup>; FluLaval<sup>®</sup>; Fluvirin<sup>®</sup>; Fluzone<sup>®</sup>

## Uses

### Prevention of Seasonal Influenza A and B Virus Infections

- Prevention of seasonal influenza virus infection in adults, adolescents, and children  $\geq 6$  months of age.
- Influenza is an acute viral infection; influenza viruses spread from person to person mainly through large-particle respiratory droplet transmission. In the US, epidemics of seasonal influenza occur annually, usually during late fall through early spring. Influenza viruses can cause illness in any age group; children have highest rate of infection. Influenza can exacerbate underlying medical conditions or lead to pneumonia in certain individuals. Individuals  $\geq 65$  years of age, children  $< 2$  years of age, and individuals with chronic medical conditions have highest risk of influenza-related complications.
- Annual vaccination is the most effective strategy for preventing seasonal influenza and its complications. Immunization efforts focus on vaccinating individuals at risk for influenza complications and contacts of these individuals.
- For prevention of seasonal influenza infection, 2 different types of influenza vaccine are commercially available in the US: intranasal vaccine containing live, attenuated virus and parenteral vaccine containing inactivated virus subunits. Both vaccine types contain influenza virus strains antigenically equivalent to the annually recommended seasonal influenza strains and are considered effective in children and adults; however, data directly comparing the efficacy of these 2 types of influenza vaccines are limited. Parenteral inactivated influenza vaccine has several advantages because it can be used in a wider age group than intranasal live influenza vaccine, including children as young as 6 months of age and adults  $\geq 50$  years. Parenteral inactivated vaccine can be used in some individuals who should not receive the intranasal vaccine, including pregnant women, individuals with underlying medical conditions that may predispose them to severe disease following influenza infection, children and adolescents receiving long-term aspirin therapy, and individuals who have close contact with severely immunocompromised individuals requiring a protective environment (e.g., hematopoietic stem cell transplant [HSCT] recipients).

### USPHS Advisory Committee on Immunization Practices (ACIP) Recommends Annual Vaccination Against Seasonal Influenza for the Following Individuals Using an Appropriate Vaccine:

All children 6 months to 18 years of age

All adults  $\geq 50$  years of age

Adults who want to reduce their risk of becoming ill with influenza or transmitting influenza to others

Children and adolescents 6 months to 18 years of age receiving long-term aspirin therapy who might therefore be at risk for Reye's syndrome after influenza infection

Women who will be pregnant during the influenza season

Children, adolescents, and adults with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, cognitive, neurologic/neuromuscular, hematologic, or metabolic disorders (including diabetes mellitus)

Children, adolescents, and adults who are immunosuppressed, including those receiving immunosuppressive drugs and those with HIV infection

Children, adolescents, or adults who are residents of nursing homes and other chronic-care facilities

Health-care workers

Household contacts and caregivers of children  $< 5$  years of age (especially contacts of children  $< 6$  months of age)

Household contacts and caregivers of adults  $\geq 50$  years of age

Household contacts and caregivers of individuals with medical conditions that put them at high risk for severe influenza complications

- Travelers who want to reduce their risk of influenza infection should receive vaccination with seasonal influenza vaccine, preferably at least 2 weeks before departure. The risk for exposure to seasonal influenza during travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year; in temperate regions of the southern hemisphere, influenza activity generally occurs from April through September; in temperate climates, travelers also may be exposed to influenza during the summer (especially when traveling as part of large tourist groups that include individuals from areas of the world where influenza is circulating). ACIP recommends that travelers (especially those at high risk for influenza complications) be vaccinated against seasonal influenza before travel if they were not vaccinated during the preceding fall or winter, will be traveling to the tropics, traveling with organized tourist groups at any time of year, or traveling to the southern hemisphere between April and September.
- HIV-infected individuals may be at high risk for influenza-related complications and should receive annual vaccination against seasonal influenza. However, antibody response may be reduced in HIV-infected individuals and is inversely correlated with severity of the disease. (See Individuals with Altered Immunocompetence under Cautions.)
- Hematopoietic stem cell transplantation (HSCT) candidates should receive seasonal influenza virus vaccine inactivated during the influenza season prior to HSCT and then annually thereafter, beginning  $\geq 6$  months after HSCT. The vaccine may not be effective if given  $< 6$  months after HSCT.
- ACIP states that students or other persons in institutional settings (e.g., those who reside in dormitories or correctional facilities) should be encouraged to receive vaccination against seasonal influenza to minimize morbidity and disruption of routine activities during epidemics. In addition, individuals who provide essential community services should be considered for annual vaccination against seasonal influenza to minimize disruption of essential activities during influenza outbreaks.
- Influenza vaccines are *not* effective against all strains of influenza, but may be effective against those strains (and closely related strains) represented in the vaccine.
- Seasonal influenza vaccines for the 2009–2010 influenza season are *not* expected to provide protection against infection with the 2009 pandemic influenza A (H1N1) virus, previously referred to as the novel 2009 influenza A (H1N1) virus or swine-origin influenza A (H1N1) virus. However, influenza A (H1N1) 2009 monovalent vaccine may be indicated in certain groups at highest risk for infection or influenza-related complications to prevent infection caused by this strain. Seasonal influenza vaccines also are *not* expected to provide protection against infection with avian influenza A viruses, including avian influenza A (H5N1). Although an inactivated influenza A (H5N1) monovalent vaccine has been approved by the FDA, the vaccine is not available commercially but has been purchased by the US Federal Government for inclusion in the National Stockpile.
- Information regarding influenza surveillance and updated recommendations for prevention and treatment of seasonal influenza is available from CDC at <http://www.cdc.gov/flu>. CDC information regarding prevention and treatment of 2009 influenza A (H1N1) is available at <http://www.cdc.gov/h1n1flu> and information regarding avian influenza A (H5N1) is available at <http://www.cdc.gov/flu/avian>.

## Dosage and Administration

### Administration

#### IM Administration

Administer by IM injection.

Do not administer IV or sub-Q.

Administer every year before exposure to seasonal influenza. Optimum time for annual vaccination against seasonal influenza cannot be determined since influenza seasons vary in timing and duration and more than one outbreak might occur in a single community in a single year. In the US, localized outbreaks indicating start of the annual influenza season can occur as early as October; peak influenza activity often occurs in January or February, but has occurred as late as April or May. Begin vaccination efforts each year as soon as the seasonal vaccine is available (usually available beginning in September or October); continue vaccination efforts throughout influenza season.

When planning influenza vaccination efforts for the 2009-2010 influenza season, consider that vaccination against the 2009 pandemic influenza A (H1N1) virus, previously referred to as the novel 2009 influenza A (H1N1) virus or swine-origin influenza A (H1N1) virus, may be indicated in addition to vaccination against seasonal influenza in certain individuals and may create additional burden on vaccination programs and health-care providers. To reduce potential overlap between vaccination against seasonal influenza and vaccination against the 2009 pandemic influenza A (H1N1) virus, ACIP recommends that immunization against seasonal influenza be initiated as soon as the seasonal vaccine is available (e.g., September).

Shake vaccine vial before withdrawing a dose. Shake prefilled syringe before administering a dose. Discard vaccine if it contains particulates, appears discolored, or cannot be resuspended with thorough agitation.

Do *not* mix with any other vaccine or solution.

To ensure delivery into muscle, IM injections should be made at a 90° angle to the skin using a needle length appropriate for the individual's age and body mass. For adults and adolescents, administer IM into the deltoid muscle. In children  $\geq 3$  years of age, IM injections should be made into the deltoid muscle if muscle mass is adequate; alternatively, the anterolateral thigh can be

used. In children 6 months to 2 years of age, IM injections should preferably be made in the anterolateral aspect of the thigh.

Do *not* administer into buttock muscle because of potential for injection-associated injury to sciatic nerve. Do *not* administer into any area where there may be a major nerve trunk.

Although some manufacturers state that aspiration (i.e., pulling back on the syringe plunger after needle insertion and before injection) can be performed to ensure that a blood vessel has not been entered, ACIP states this procedure is not required because large blood vessels are not present at recommended IM injection sites.

May be given simultaneously with other vaccines during same health-care visit. (See Other Vaccines under Interactions.) When multiple vaccines are administered during a single health-care visit, each vaccine should be given with a different syringe and at different injection sites. Separate injection sites by at least 1 inch (if anatomically feasible) to allow appropriate attribution of any local adverse effects that may occur.

## Dosage

Dose and dosing schedule for prevention of seasonal influenza depend on individual's age, vaccination status, and specific product administered.

A single-dose regimen is used in adults and children  $\geq 9$  years of age. To promote an adequate antibody response, a 2-dose regimen is used in children 6 months to 8 years of age who have not previously received seasonal influenza vaccine or received seasonal influenza vaccine for the first time during the previous season and did not receive a second dose during the same season.

Afluria<sup>®</sup>, Fluarix<sup>®</sup>, and FluLaval<sup>®</sup> are used *only* in adults  $\geq 18$  years of age.

Fluzone<sup>®</sup> may be used in adults, adolescents, and children  $\geq 6$  months of age. Fluvirin<sup>®</sup> may be used in adults, adolescents, and children  $\geq 4$  years of age.

## Pediatric Patients

### Prevention of Seasonal Influenza A and B Virus Infections

#### >Children and Adolescents 6 Months to 18 Years of Age (Fluzone<sup>®</sup>)

**IM:** Children 6–35 months of age who have not previously received seasonal influenza vaccine or received seasonal influenza vaccine for the first time during the previous season and did not receive a second dose during the same season: Two 0.25-mL doses administered at least 1 month apart.

Children 6–35 months of age who received 2 doses of seasonal influenza vaccine during the previous season or at least 1 dose of seasonal influenza vaccine 2 or more years ago: Single 0.25-mL dose.

Children 3–8 years of age who have not previously received seasonal influenza vaccine or received seasonal influenza vaccine for the first time during the previous season and did not receive a second dose during the same season: Two 0.5-mL doses administered at least 1 month apart.

Children 3–8 years of age who received 2 doses of seasonal influenza vaccine during the previous season or at least 1 dose of seasonal influenza vaccine 2 or more years ago: Single 0.5-mL dose.

Children and adolescents 9–18 years of age: Single 0.5-mL dose.

#### >Children and Adolescents 4–18 Years of Age (Fluvirin<sup>®</sup>)

**IM:** Children 4–8 years of age who have not previously received seasonal influenza vaccine or received seasonal influenza vaccine for the first time during the previous season and did not receive a second dose during the same season: Two 0.5-mL doses administered at least 1 month apart.

Children 4–8 years of age who received 2 doses of seasonal influenza vaccine during the previous season or at least 1 dose of seasonal influenza vaccine 2 years ago: Single 0.5-mL dose.

Children and adolescents 9–18 years of age: Single 0.5-mL dose.

## Adults

### Prevention of Seasonal Influenza A and B Virus Infections

**IM:** Single 0.5-mL dose.

## Special Populations

### Hepatic Impairment

No specific dosage recommendations.

### Renal Impairment

No specific dosage recommendations.

### Geriatric Patients

No specific dosage recommendations. (See Geriatric Use under Cautions.)

# Cautions

## Contraindications

- Hypersensitivity to egg or egg proteins or any vaccine component. (See Sensitivity Reactions under Cautions.)
- Life-threatening reaction to previous dose of any influenza vaccine.
- Afluria<sup>®</sup>: Hypersensitivity to neomycin or polymyxin. (See Neomycin and/or Polymyxin B Allergy under Cautions.)

## Warnings/Precautions

## Sensitivity Reactions

### Hypersensitivity Reactions

Immediate, presumably allergic reactions (e.g., urticaria, angioedema, anaphylaxis, allergic asthma) reported rarely. Reactions may result from sensitivity to some vaccine component; the majority of reactions most likely are related to residual egg protein.

Seasonal parenteral inactivated influenza vaccine is produced using embryonated chicken eggs and can contain residual egg protein that may induce immediate hypersensitivity reactions, including anaphylaxis, in individuals with severe egg allergy. ACIP states asking patients if they can eat eggs without adverse effects is a reasonable way to identify those who may be at risk for allergic reactions if they receive the vaccine. Those who are able to eat eggs or egg products safely usually can receive the vaccine; those with a history of anaphylactic or other immediate hypersensitivity reaction (e.g., hives, angioedema, allergic asthma) to eggs or egg proteins should *not* receive the vaccine. (See Contraindications under Cautions.)

Prior to administration, review patient's history with respect to possible hypersensitivity to vaccine components, including egg and egg products. Epinephrine and other appropriate agents should be readily available in case anaphylaxis occurs.

Do *not* administer additional vaccine doses to any individual who experienced life-threatening reactions to a previous dose. (See Contraindications under Cautions.)

### Neomycin and/or Polymyxin B Allergy

Afluria<sup>®</sup>: Contains trace amounts of neomycin sulfate ( $\leq 0.2$  picograms) and polymyxin B ( $\leq 0.03$  picograms). Manufacturer states the vaccine is contraindicated in individuals hypersensitive to neomycin or polymyxin.

Fluvirin<sup>®</sup>: Contains neomycin sulfate ( $\leq 2.5$  mcg) and polymyxin B ( $\leq 3.75$  mcg).

Neomycin allergy usually results in delayed-type (cell-mediated) hypersensitivity reactions manifested as contact dermatitis. ACIP and AAP state that vaccines containing trace amounts of neomycin should not be used in individuals with a history of anaphylactic reaction to neomycin, but may be considered in those with a history of delayed-type neomycin hypersensitivity if benefits of vaccination outweigh risks.

### Thimerosal Allergy

All multiple-dose vials of influenza virus vaccine contain thimerosal as a preservative; some preparations of the vaccine in prefilled syringes are preservative-free but contain trace amounts of thimerosal from the manufacturing process. (See Thimerosal Precautions under Cautions.) Hypersensitivity reactions to thimerosal contained in vaccines have been reported in some individuals. These reactions usually manifest as local, delayed-type hypersensitivity reactions (e.g., erythema, swelling), but a generalized reaction manifested as pruritus and an erythematous, maculopapular rash on all 4 extremities has been reported rarely. Even when patch or intradermal tests for thimerosal sensitivity are positive, most individuals do not develop hypersensitivity reactions to thimerosal administered as a component of vaccines.

ACIP states that a history of delayed-type hypersensitivity to thimerosal is not a contraindication to use of vaccines that contain thimerosal.

### Latex Sensitivity

Fluarix<sup>®</sup>: Some components (i.e., tip cap, plunger) of the single-dose prefilled syringes contain dry natural latex.

Some individuals may be hypersensitive to natural latex proteins. Take appropriate precautions if this preparation is administered to individuals with a history of latex sensitivity.

### Guillain-Barré Syndrome

Carefully consider possible benefits and potential risks of influenza vaccine in individuals who experienced Guillain-Barré syndrome (GBS) within 6 weeks of previous influenza vaccination.

Unclear whether influenza vaccination increases risk of recurrence of GBS. AAP states that influenza vaccines should not be used in children who developed GBS within 6 weeks after a dose of any influenza vaccine. ACIP states that benefits of influenza vaccine may outweigh risks in individuals with a history of GBS who are at high risk for severe influenza-related complications. However, it may be prudent to avoid influenza vaccine in individuals who are not at high risk for severe influenza complications if they experienced GBS within 6 weeks after previous influenza vaccination.

### Individuals with Altered Immunocompetence

May be administered to individuals immunosuppressed as the result of disease or immunosuppressive therapy. Consider possibility that immune response to the vaccine and efficacy may be reduced in these individuals.

CDC, National Institutes of Health (NIH), IDSA, AAP, and other experts state that HIV-infected children, adolescents, and adults should receive annual vaccination against seasonal influenza; however, the parenteral inactivated influenza vaccine (not the intranasal live vaccine) should be used for prevention of seasonal influenza in HIV-infected individuals. Data are limited regarding safety of parenteral inactivated influenza vaccine in HIV-infected individuals, but there is no evidence that use of the vaccine has any clinically important effect on HIV infection or immunocompetence. An adequate antibody response to parenteral inactivated influenza vaccine may be attained in HIV-infected individuals with minimal AIDS-related symptoms and normal or near normal CD4<sup>+</sup> T-cell counts. Antibody response may be inversely correlated with severity of the disease. Although parenteral inactivated influenza vaccine has been highly effective in preventing symptomatic, laboratory-confirmed influenza infection in HIV-infected individuals with mean CD4<sup>+</sup> T-cell counts of 400/mm<sup>3</sup>, the vaccine may be less effective in those with more

advanced disease and lower CD4<sup>+</sup> T-cell counts (e.g., <100/mm<sup>3</sup>). A second dose of influenza vaccine does not appear to improve immune response in these individuals.

May not be effective if given <6 months after HSCT.

Limited data indicate the vaccine does not appear to adversely affect allograft function or cause rejection episodes in kidney, heart, or liver transplant recipients. However, the vaccine may be less immunogenic in some solid organ transplant recipients, especially those vaccinated within 4 months after liver transplant.

### **Thimerosal Precautions**

Although there is no convincing evidence that the low concentrations of thimerosal (a mercury-containing preservative) contained in some vaccines is harmful to vaccine recipients, efforts to eliminate or reduce the thimerosal content in vaccines is recommended as a prudent measure to reduce mercury exposure in infants and children and part of an overall strategy to reduce mercury exposures from all sources, including food and drugs.

As a result of efforts initiated in 1999 to remove or reduce thimerosal in vaccines and expedite development and approval of preservative-free formulations of vaccines, inactivated influenza vaccine now is commercially available in prefilled syringes as preservative-free formulations that do not contain thimerosal and in prefilled syringes as preservative-free formulations that contain only trace amounts of thimerosal from the manufacturing process (≤1 mcg of mercury per 0.5-mL dose). FDA states that trace amounts of thimerosal from the manufacturing process are not considered clinically important. Only multiple-dose vials of inactivated influenza virus still contain thimerosal as a preservative (≤ 25 mcg of mercury per 0.5-mL dose). Intranasal live influenza vaccine does not contain thimerosal.

Although it was suggested that thimerosal in vaccines theoretically could have adverse effects in vaccine recipients, there is no conclusive evidence that the low levels of thimerosal contained in vaccines cause harm in vaccine recipients. A link between thimerosal in vaccines and neurodevelopmental disorders in children (autism, attention deficit/hyperactivity disorder [ADHD], speech or language delay) possibly related to mercury neurotoxicity has been theorized; however, considerable evidence has accumulated that supports the absence of substantial risk for neurodevelopmental disorders or other harm resulting from exposure to thimerosal-containing vaccines. In 2004, the Immunization Safety Review Committee of the IOM examined the hypothesis that thimerosal-containing vaccines are causally associated with autism and concluded that the body of epidemiologic evidence favors rejection of a causal relationship between these vaccines and autism.

Analysis of adverse effects reported to the Vaccine Adverse Event Reporting System (VAERS) indicates that there is no difference in the incidence of injection site reactions, rash, or infections in infants 6–23 months of age who received preservative-containing (thimerosal-containing) inactivated influenza vaccine compared with those who received preservative-free preparations of the vaccine. To date, the only adverse effects known to be caused by thimerosal contained in vaccines are hypersensitivity reactions. (See Thimerosal Allergy under Cautions.)

USPHS, ACIP, AAP, AAFP, and other experts state that use of vaccines that contain thimerosal is preferable to withholding vaccination since failure to provide protection against vaccine-preventable diseases may represent an immediate threat, especially in infants. ACIP states that benefits of influenza vaccination for all recommended groups (including pregnant women and young children) outweigh concerns related to theoretical risks of thimerosal exposure from vaccination with preparations containing thimerosal. AAP states that the benefits of protecting children (including children at high risk with underlying CNS disorders) outweigh the hypothetical risks associated with the minute amounts of thimerosal contained in some currently available influenza vaccine preparations.

Afluria<sup>®</sup>: Commercially available in 0.5-mL prefilled syringes as a preservative-free formulation (thimerosal not used in manufacturing process). Also available in multiple-dose vials containing thimerosal as a preservative (24.5 mcg of mercury per 0.5-mL dose).

Fluarix<sup>®</sup>: Commercially available in 0.5-mL prefilled syringes as a preservative-free formulation that does not contain thimerosal.

FluLaval<sup>®</sup>: Commercially available in multiple-dose vials containing thimerosal as a preservative (25 mcg of mercury per 0.5 mL).

Fluvirin<sup>®</sup>: Commercially available in prefilled syringes in a preservative-free formulation containing only trace amounts of thimerosal from the manufacturing process (≤1 mcg of mercury per 0.5 mL). Also available in multiple-dose vials containing thimerosal as a preservative (25 mcg of mercury per 0.5-mL dose).

Fluzone<sup>®</sup>: Commercially available in 0.25- and 0.5-mL prefilled syringes and single-dose 0.5-mL vials as a preservative-free formulation (thimerosal not used in manufacturing process). Also available in multiple-dose vials containing thimerosal as a preservative (25 mcg of mercury per 0.5-mL dose).

### **Limitations of Vaccine Effectiveness**

May require up to 2 weeks for protection to develop following seasonal influenza vaccination.

May not protect all vaccine recipients against influenza.

Seasonal influenza vaccine is formulated annually to contain influenza A and B antigens predicted to represent strains of influenza virus likely to circulate in the US during the upcoming influenza season. (See Actions.) Efficacy of the seasonal vaccine during any given year depends on how closely viral strains represented in the vaccine match viral strains circulating during the season.

Seasonal inactivated influenza vaccine for the 2009–2010 influenza season is *not* expected to provide protection against the 2009 pandemic influenza A (H1N1) virus, previously referred to as the novel 2009 influenza A (H1N1) virus or swine-origin influenza A (H1N1) virus, nor against infection with avian influenza A viruses, including avian influenza A (H5N1).

### **Duration of Immunity**

Immunity declines during the year after seasonal influenza vaccination. In addition, circulating strains of seasonal influenza virus change from year to year. Annual vaccination is needed for prevention of seasonal influenza.

Do *not* administer vaccine from a previous influenza season in an attempt to provide protection during a subsequent influenza season.

### **Concomitant Illness**

Delay administration in individuals with moderate to severe acute febrile illness until symptoms have subsided. ACIP states that minor acute illness (with or without fever), generally does not preclude vaccination.

### **Individuals with Bleeding Disorders**

Because bleeding may occur following IM administration in individuals with thrombocytopenia or a bleeding disorder (e.g., hemophilia) or in those receiving anticoagulant therapy, use caution in such individuals.

ACIP states that vaccines may be given IM to individuals who have bleeding disorders or are receiving anticoagulant therapy if a clinician familiar with the patient's bleeding risk determines that the preparation can be administered with reasonable safety. In these cases, use a fine needle (23 gauge) to administer the vaccine and apply firm pressure to the injection site (without rubbing) for ≥2 minutes. If patient is receiving antihemophilia therapy, administer the IM vaccine shortly after a scheduled dose of such therapy.

Advise individual and/or their family about the risk of hematoma from IM injections.

### **Improper Storage and Handling**

Improper storage or handling of vaccines may result in loss of vaccine potency and reduced immune response in vaccinees.

Inspect all vaccines upon delivery and monitor during storage to ensure that the appropriate temperature is maintained.

Do *not* administer vaccine that has been mishandled or has not been stored at the recommended temperature. (See Storage under Stability.) If there are concerns about mishandling, contact the manufacturer or state or local health departments for guidance on whether the vaccine is usable.

### **Specific Populations**

#### **Pregnancy**

Category C.

Manufacturers state that the vaccine should be used in pregnant women only when clearly needed.

Because pregnant women are at risk for influenza complications, ACIP and other experts recommend that all women who are pregnant or will be pregnant during influenza season receive inactivated influenza vaccine for prevention of seasonal influenza, including those without underlying influenza risk factors. ACIP states that the inactivated vaccine can be administered during any trimester.

ACIP, American College of Obstetricians and Gynecologists (ACOG), American College of Physicians (ACP), NIH, IDSA, and other experts state that parenteral inactivated influenza vaccine (not intranasal live influenza vaccine) should be used for prevention of seasonal influenza in pregnant women.

ACIP states that benefits of influenza vaccination for pregnant women outweigh theoretical risks from thimerosal exposure by vaccination with preparations containing thimerosal; no preference is indicated for use of inactivated influenza vaccine preparations that do not contain thimerosal as a preservative. (See Thimerosal Precautions under Cautions.)

#### **Lactation**

Not known whether parenteral inactivated influenza vaccine is distributed into milk. Manufacturers recommend caution.

Inactivated vaccines do not affect safety of breastfeeding for lactating women or their infants. ACIP and CDC state that breastfeeding does not adversely affect immune response and is not a contraindication to vaccination.

#### **Pediatric Use**

Afluria<sup>®</sup>, Fluarix<sup>®</sup>, and FluLaval<sup>®</sup>: Safety and efficacy not established in children <18 years of age.

Fluvirin<sup>®</sup>: Safety and efficacy not established in children <4 years of age.

Fluzone<sup>®</sup>: Safety and efficacy not established in infants <6 months of age.

ACIP states that benefits of influenza vaccination for children outweigh theoretical risks from thimerosal exposure by vaccination with preparations containing thimerosal and any available age-appropriate inactivated influenza vaccine can be used in children. AAP states that the benefits of protecting children against the known risks of influenza outweigh the hypothetical risks associated with the minute amounts of thimerosal contained in some currently available influenza vaccine preparations. (See Thimerosal Precautions under Cautions.)

Because seasonal inactivated influenza vaccine is not indicated in infants <6 months of age, all household and other close contacts (e.g., day-care providers) of infants <6 months of age

should be vaccinated against seasonal influenza using vaccine appropriate for their age and target group since this may provide some protection against seasonal influenza for these young infants.

### Geriatric Use

No substantial differences in safety relative to younger adults; may be less immunogenic in geriatric individuals.

### Common Adverse Effects

Injection site reactions (i.e., tenderness, pain, redness, swelling), headache, fatigue, myalgia, fever, malaise.

## Drug Interactions

### Other Vaccines

Although specific studies may not be available evaluating concurrent administration with each antigen, simultaneous administration with other age-appropriate vaccines, including live virus vaccines, toxoids, or inactivated or recombinant vaccines, during the same health-care visit is not expected to affect immunologic response or adverse reactions to any of the preparations. Immunization with parenteral inactivated influenza vaccine can be integrated with immunization against diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (HIB), hepatitis A, hepatitis B, human papillomavirus (HPV), poliovirus, measles, mumps, rubella, rotavirus, meningococcal disease, pneumococcal disease, and varicella. However, each vaccine should be administered using a different syringe and different injection site. In addition, ACIP states that seasonal inactivated influenza vaccine and inactivated influenza A (H1N1) 2009 monovalent vaccine may be administered simultaneously if different anatomic sites are used.

### Specific Drugs

Drug	Interaction	Comments
<b>Aldesleukin</b>	Possible increased antibody response to influenza vaccine in geriatric adults	
<b>Anticoagulants (e.g., warfarin)</b>	Increased PT, GI bleeding, hematuria, muscle hematoma, epistaxis reported rarely  Potential to inhibit warfarin clearance	Consider possible interaction in individuals receiving warfarin; some clinicians suggest closely monitor for enhanced anticoagulant effects (See Individuals with Bleeding Disorders under Cautions)
<b>Antiviral agents active against influenza (amantadine, rimantadine, oseltamivir, zanamivir)</b>	Amantadine, rimantadine, zanamivir: No interference with antibody response to parenteral inactivated influenza vaccine  Oseltamivir: No specific studies, but interference with antibody response to parenteral inactivated influenza vaccine not expected; oseltamivir does not interfere with humoral antibody response to influenza infection	Amantadine, rimantadine, oseltamivir, zanamivir: May be used concomitantly with parenteral inactivated influenza vaccine if indicated  Oseltamivir: May be administered simultaneously with or at any interval before or after parenteral inactivated influenza vaccine
<b>Aspirin</b>	Possible increased antibody response to influenza vaccine in geriatric adults	
<b>Immune globulin (immune globulin IM [IGIM], immune globulin IV [IGIV]) or specific immune globulin (hepatitis B immune globulin [HBIG], rabies immune globulin [RIG], tetanus immune globulin [TIG], varicella zoster immune globulin [VZIG])</b>	No evidence that immune globulin preparations interfere with immune response to inactivated vaccines	Parenteral inactivated influenza vaccine may be given simultaneously with or at any interval before or after immune globulin preparations

### Immunosuppressive agents (e.g., alkylating agents, antimetabolites, corticosteroids, radiation)

Potential for decreased antibody response  
  
Corticosteroid therapy (prednisone or equivalent) in a dosage  $\geq 2$  mg/kg daily or  $\geq 20$  mg daily given for  $\geq 2$  weeks is considered immunosuppressive

Children with malignant neoplasms: Administer influenza vaccine  $\geq 3$  weeks after chemotherapy is completed and peripheral granulocytes and lymphocyte counts are  $>1000/mL$

Consider deferring vaccination during short-term, high-dose corticosteroid therapy

Parenteral inactivated influenza vaccine may be administered to those receiving long-term immunosuppressive therapy

### Influenza A (H1N1) 2009 monovalent vaccine

Parenteral inactivated influenza A (H1N1) 2009 monovalent vaccine: May be administered simultaneously with seasonal parenteral inactivated influenza vaccine if different anatomic sites are used

Intranasal live influenza A (H1N1) 2009 monovalent vaccine: Data not available regarding concomitant administration with seasonal parenteral inactivated influenza vaccine

### Phenytoin

Possible pharmacokinetic interaction (both increased and decreased serum concentrations of phenytoin reported); potential inhibition of phenytoin clearance

Consider possible interaction in individuals receiving phenytoin

### Pneumococcal vaccine

PPSV23 (Pneumovax<sup>®</sup> 23): Simultaneous administration with parenteral inactivated influenza vaccine does not interfere with the immune response or increase adverse effects of either vaccine

PPSV23 (Pneumovax<sup>®</sup> 23): May be administered simultaneously with parenteral inactivated influenza vaccine using different syringes and different injection sites

PCV7 (Pneumovax<sup>®</sup>): May be administered simultaneously with parenteral inactivated influenza vaccine using different syringes and different injection sites

### Theophylline

Potential interaction (clearance of theophylline inhibited)

Clinical importance unknown; consider possible interaction in individuals receiving theophylline

### Zoster vaccine (ZOS)

Concurrent administration of parenteral inactivated influenza vaccine and zoster vaccine live in adults  $\geq 50$  years of age results in antibody responses and adverse effects similar to those reported when the vaccines are

May be given concurrently (using different syringes and different injection sites) or at any interval before or after zoster vaccine

administered 4 weeks apart

## Stability

### Storage

#### Parenteral

##### Injectable Suspension, for IM Use

2–8°C; do not freeze. If freezing occurs, discard vaccine; potency of the vaccine destroyed by freezing.

Return multiple-dose vials to 2–8°C between uses. Discard if not used by the expiration date noted on the vial.

Protect from light.

Depending on the manufacturer, single-dose syringes and vials are preservative-free or contain only trace amounts of thimerosal from the manufacturing process. Multiple-dose vials contain thimerosal as a preservative. (See Thimerosal Precautions under Cautions.)

## Actions

- Inactivated influenza virus vaccines that are used for prevention of seasonal influenza are trivalent vaccines containing noninfectious, sterile suspensions of suitably inactivated influenza virus types A and B subunits.
- Inactivated influenza vaccines commercially available in the US for prevention of seasonal influenza are prepared from formaldehyde- or propiolactone-inactivated influenza viruses harvested from allantoic fluids of chick embryos infected with the viruses and are split-virus preparations (i.e., contain purified subvirion or purified surface antigen).
- Influenza vaccines used for prevention of seasonal influenza are formulated annually to contain influenza A (H3N2), influenza A (H1N1), and influenza B viruses likely to circulate in the US during the next influenza season.
- The 2009–2010 seasonal parenteral inactivated influenza vaccine for the US contains A/Brisbane/59/2007, IVR-148 (H1N1); A/Uruguay/716/2007, NYMC X-175C (H3N2) (A/Brisbane/10/2007-like); and B/Brisbane/60/2008.
- Only 1 of 3 antigens contained in the 2009–2010 seasonal influenza vaccine (the influenza type B component) differs from the antigens contained in the vaccine used during the previous influenza season (2008–2009).
- Regardless of manufacturer, all parenteral inactivated influenza vaccines commercially available in the US for prevention of seasonal influenza contain the same influenza antigens and these seasonal inactivated vaccines are antigenically equivalent to the seasonal intranasal live influenza vaccine.
- Influenza vaccines stimulate active immunity to influenza virus strains represented in the vaccine.
- Efficacy of influenza vaccine in preventing seasonal influenza virus infection depends on whether the virus strains represented in the vaccine are antigenically similar to influenza virus strains circulating during the influenza season.
- When there is a good match between the vaccine formulation and circulating strains, a protective effect generally is achieved in 70–90% of healthy adults <65 years of age.
- Immune response to the seasonal influenza vaccine may be lower in geriatric individuals, very young children, or individuals who are immunocompromised or have certain chronic medical conditions.
- Seasonal influenza vaccines for the 2009–2010 influenza season are *not* expected to provide protection against the 2009 pandemic influenza A (H1N1) virus, previously referred to as novel 2009 influenza A (H1N1) or swine-origin influenza A (H1N1) virus, and are *not* expected to provide protection against infection with avian influenza A viruses, including avian influenza A (H5N1).

## Advice to Patients

- Prior to administration of seasonal parenteral inactivated influenza vaccine, provide a copy of the appropriate CDC Vaccine Information Statement (VIS) to the patient or patient's legal representative (VISs are available at <http://www.cdc.gov/vaccines/pubs/vis/default.htm>).
- Advise patients that parenteral, inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza.
- Advise patients that parenteral, inactivated influenza vaccine provides protection against illness due to influenza viruses only and cannot provide protection against all respiratory illness.
- Advise patient and/or patient's parent or guardian of the risks and benefits of vaccine administration.
- Importance of annual vaccination against seasonal influenza.
- Advise patient and/or patient's parent or guardian that a single dose of seasonal influenza vaccine is necessary each year in adults, adolescents, and older children, but that 2 doses of seasonal influenza vaccine are necessary in children 6 months to 8 years of age who have not previously received 2 doses of any seasonal influenza vaccine in a single influenza season.

- Importance of informing clinicians of adverse effects. Clinicians or individuals can report any adverse reactions that occur following vaccination to the Vaccine Adverse Event Reporting System (VAERS) at 800-822-7967 or <http://www.vaers.hhs.gov/>.
- Importance of informing clinician of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as concomitant medical problems (e.g., GBS).
- Importance of women informing clinician if they are or plan to become pregnant or plan to breast-feed.
- Importance of informing patients of other precautionary information. (See Cautions.)

## Preparations

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

### Influenza Virus Vaccine Inactivated (2009–2010)

#### Parenteral

Injectable suspension, for IM use

15 mcg hemagglutinin each of A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2) (A/Brisbane/10/2007-like), and B/Brisbane/60/2008 per 0.5 mL

**Afluria**<sup>®</sup> (preservative-free; available in 0.5 mL prefilled disposable syringes or with thimerosal [24.5 mcg of mercury per 0.5 mL]; available in multiple-dose vials), CSL Biotherapies

**Fluarix**<sup>®</sup> (preservative-free; available in 0.5 mL prefilled disposable syringes), GlaxoSmithKline

**FluLaval**<sup>®</sup> (with thimerosal [25 mcg of mercury per 0.5 mL]; available in multiple-dose vials), GlaxoSmithKline

**Fluvirin**<sup>®</sup> (preservative-free with thimerosal [ $\leq$ 1 mcg of mercury per 0.5 mL]; available in 0.5 mL prefilled disposable syringes or with thimerosal [25 mcg of mercury per 0.5 mL]; available in multiple-dose vials), Novartis Vaccines

**Fluzone**<sup>®</sup> (preservative-free; available in 0.25 mL prefilled disposable syringes, 0.5 mL prefilled disposable syringes, and 0.5 mL vials or with thimerosal [25 mcg of mercury per 0.5 mL]; available in multiple-dose vials), Sanofi Pasteur