

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

Brands: Afluria[®]; Fluarix[®]; Flulaval[®]; Fluvirin[®]; Fluzone[®]

Uses

Prevention of Seasonal Influenza A and B Virus Infections

- Prevention of seasonal influenza virus infection in adults, adolescents, and infants and children ≥ 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 ≥ 65 years of age, children < 2 years of age, and individuals with chronic medical conditions have highest risk of influenza-related complications and death.
- Annual vaccination is the most effective strategy for preventing seasonal influenza and its complications.
- The US Public Health Service Advisory Committee on Immunization Practices (ACIP) recommends routine influenza vaccination for *all* adults, adolescents, and infants and children 6 months of age or older using an age-appropriate seasonal influenza vaccine, unless contraindicated. However, seasonal influenza vaccination efforts should continue to target individuals at higher risk of influenza or influenza-related complications and those who live with or care for such individuals (e.g., health-care personnel, household or other close contacts). (See Table 1.) Targeted vaccination efforts are especially important during periods when the supply of seasonal influenza vaccine is limited.

Table 1. ACIP Recommends Targeted Seasonal Influenza Vaccination Efforts in the Following Individuals Using an Appropriate Vaccine:

Infants and children 6 months to < 5 years of age (59 months)
Adults ≥ 50 years of age
Adults, adolescents, and children ≥ 6 months of age with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
Adults, adolescents, and children ≥ 6 months of age who are immunosuppressed, including those receiving immunosuppressive drugs and those with HIV infection
Women who are or will be pregnant during the influenza season
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
Adults, adolescents, and children ≥ 6 months of age who are residents of nursing homes and other chronic-care facilities
American Indians and Alaska Natives
Morbidly obese individuals (body mass index ≥ 40)
Health-care personnel
Household contacts and caregivers of children < 5 years of age (especially contacts of infants < 6 months of age)
Household contacts and caregivers of adults ≥ 50 years of age
Household contacts and caregivers of individuals with medical conditions that put them at high risk for severe influenza complications

- 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. Parenteral inactivated influenza vaccine has several advantages because it can be used in a wider age group than intranasal live influenza vaccine, including infants

as young as 6 months of age and adults ≥ 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).

- Travelers who want to reduce their risk of influenza infection should receive vaccination with seasonal influenza vaccine at least 2 weeks before departure. Risk for exposure to seasonal influenza during travel depends on the time of year and destination. In tropical and subtropical areas, influenza occurs throughout the year. In temperate regions, influenza activity generally occurs from October to May in the northern hemisphere and from April through September in the southern hemisphere. However, travelers may be exposed to influenza at any time of the year if they are traveling on a cruise or as part of a large tourist group that includes 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.)
- HSCT candidates should receive seasonal influenza virus vaccine inactivated during the influenza season prior to HSCT and then annually thereafter, beginning ≥ 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.
- Seasonal influenza vaccine is *not* effective against all strains of influenza, but may be effective against those strains (and closely related strains) represented in the vaccine.
- The 2009 influenza A (H1N1) virus, previously referred to as the novel 2009 influenza A (H1N1) virus or swine-origin influenza A (H1N1) virus, is likely to continue to circulate during the 2011–2012 season. Seasonal influenza vaccine for the 2011–2012 influenza season is expected to provide protection against the 2009 influenza A (H1N1) virus and influenza A (H3N2) and influenza B viruses represented in the vaccine.
- Seasonal influenza vaccine is *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>.

Dosage and Administration

Administration

Afluria[®], Fluarix[®], Fluvirin[®], Fluzone[®], Fluzone[®] High-Dose: Administer by IM injection. Do *not* administer IV, sub-Q, or intradermally; do *not* administer using a jet injector.

Fluzone[®] Intradermal: Administer intradermally.

Administer every year before exposure to seasonal influenza. Begin annual vaccination efforts by October (or as soon as the seasonal influenza vaccine is available); continue vaccination efforts throughout influenza season (even in December or after influenza activity has begun in the community). In the US, localized influenza outbreaks indicating start of 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.

May be given simultaneously with other age-appropriate vaccines during same health-care visit. (See Interactions.) When multiple vaccines are administered during a single health-care visit, each parenteral 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.

Since syncope may occur following vaccination, observe vaccinees for approximately 15 minutes after the dose. Syncope occurs most frequently in adolescents and young adults. Syncope and secondary injuries may be averted if vaccinees sit or lie down during and for 15 minutes after vaccination. If syncope occurs, observe patient until symptoms resolve.

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

Discard vaccine if it contains particulates, appears discolored, or cannot be resuspended with thorough agitation.

IM Administration

Shake vaccine vial before withdrawing a dose. Shake prefilled syringe before administering a dose.

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 ≥3 years of age, IM injections should preferably be made into the deltoid muscle; alternatively, the anterolateral thigh can be used. In children 6 months to 2 years of age, IM injections should preferably be made into the anterolateral thigh; alternatively, the deltoid muscle can be used in those 1–2 years of age if muscle mass is adequate.

Do *not* administer into gluteal region or any area where there may be a major nerve trunk. If the gluteal muscle is chosen for infants <12 months of age because of special circumstance (e.g., physical obstruction of other sites), it is *essential* to identify anatomical landmarks prior to injection.

Intradermal Administration

Fluzone® Intradermal is the *only* commercially available influenza vaccine for intradermal use.

Gently shake the prefilled microinjection system prior to administration.

Administer intradermal injections into the region of deltoid muscle with the needle at a 90° angle to the skin. Consult manufacturer's labeling for more detailed administration instructions.

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 of seasonal influenza vaccine is used in adults, adolescents, and children ≥9 years of age.

A 2-dose regimen of seasonal influenza vaccine is necessary in infants and children 6 months through 8 years of age who have *not* previously received any doses of seasonal influenza vaccine or have an *uncertain* history regarding influenza vaccination during the prior season. (See Pediatric Dosage under Dosage and Administration.)

Fluzone® is used in adults, adolescents, and infants and children ≥6 months of age.

Fluvirin® is used in adults, adolescents, and children ≥4 years of age.

Fluarix® may be used in adults, adolescents, and children ≥3 years of age.

Although Afluria® is labeled for use in adults, adolescents, and children ≥5 years of age, ACIP recommends that this vaccine be used *only* in adults, adolescents, and children ≥9 years of age. (See Pediatric Use under Cautions.)

Flulaval® is used *only* in adults ≥18 years of age.

Fluzone® Intradermal is used *only* in adults 18–64 years of age.

Fluzone® High-Dose is used *only* in adults ≥65 years of age. (See Geriatric Use under Cautions.)

Pediatric Patients

Prevention of Seasonal Influenza A and B Virus Infections

>Infants and Children 6 Months through 35 Months of Age (Fluzone®)

IM: Has *not* previously received any doses of any type of seasonal influenza vaccine or has an *uncertain* history regarding influenza vaccination during the previous influenza season: Two 0.25-mL doses administered at least 1 month apart. Received at least 1 dose of any type of seasonal influenza vaccine during the previous influenza season: ACIP and AAP recommend a single 0.25-mL dose. Manufacturer states that a single 0.25-mL dose may be used in those who received 2 doses of any influenza vaccine during the previous influenza season or at least one dose 2 or more years ago, but that two 0.25-mL doses should be administered at least 1 month apart in those who were vaccinated for the first time last season and received only a single dose at that time.

>Children 3 through 8 Years of Age (Fluarix®, Fluzone®), Children 4 through 8 Years of Age (Fluvirin®), or Children 5 through 8 Years of Age (Afluria®)

IM: Has *not* previously received any doses of any type of seasonal influenza vaccine or has an *uncertain* history regarding influenza vaccination during the previous influenza season: Two 0.5-mL doses administered at least 1 month apart. Received at least 1 dose of any type of seasonal influenza vaccine during the previous influenza season: ACIP and AAP recommend a single 0.5-mL dose. Manufacturers state that a single 0.5-mL dose may be used in those who received 2 doses of any influenza vaccine during the previous influenza season or at least one dose 2 or more years ago, but that two 0.5-mL doses should be administered at least 1 month apart in those who were vaccinated for the first time last season and received only a single dose at that time.

>Children and Adolescents 9 through 17 Years of Age (Afluria®, Fluarix®, Fluvirin®, Fluzone®)
IM: Single 0.5-mL dose.

Adults

Prevention of Seasonal Influenza A and B Virus Infections

>Adults ≥18 Years of Age (Afluria®, Fluarix®, Flulaval®, Fluvirin®, Fluzone®)
IM: Single 0.5-mL dose.

>Adults 18 through 64 Years of Age (Fluzone® Intradermal)
Intradermal: Single 0.1-mL dose.

Special Populations

Hepatic Impairment

No specific dosage recommendations.

Renal Impairment

No specific dosage recommendations.

Geriatric Patients

A standard-dose IM preparation *or* IM Fluzone® High-Dose may be used. (See Geriatric Use under Cautions.)

Standard-dose Preparations (Afluria®, Fluarix®, Flulaval®, Fluvirin®, Fluzone®)

No special dosage recommendations.

Fluzone® High-Dose

Geriatric adults ≥65 years of age: Single 0.5-mL IM dose.

Cautions

Contraindications

- History of severe or life-threatening hypersensitivity (e.g., anaphylaxis) to egg protein (eggs or egg products) or any vaccine component. (See Sensitivity Reactions under Cautions.)
- History of severe or life-threatening reaction to previous dose of any influenza vaccine.
- Afluria®: Hypersensitivity to neomycin or polymyxin. (See Neomycin and/or Polymyxin B Allergy under Cautions.)

Warnings/Precautions

Sensitivity Reactions

Immediate, presumably allergic reactions (e.g., urticaria, angioedema, anaphylaxis, anaphylactic shock, 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.

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.)

Egg Allergy

All currently available seasonal parenteral inactivated influenza vaccines are produced using embryonated chicken eggs; and can contain residual egg protein (ovalbumin) may induce immediate hypersensitivity reactions (e.g., anaphylaxis) in individuals with severe egg allergy.

ACIP states that patients who are able to eat lightly cooked eggs (e.g., scrambled eggs) without reaction are unlikely to be allergic and may receive influenza vaccination per usual protocols. However, tolerance to egg-containing foods does not exclude the possibility of egg allergy since some egg-allergic individuals may tolerate egg in baked products (e.g., bread, cake). Egg allergy can be confirmed by a consistent history of adverse reactions to eggs and egg-containing foods in addition to skin and/or blood testing for immunoglobulin E antibodies to egg proteins.

ACIP and AAP state that individuals who have less severe reactions (i.e., hives only) after eating eggs or egg-containing foods may receive influenza vaccine; however, parenteral inactivated influenza vaccine is preferred over intranasal live influenza vaccine since data are lacking regarding use of the live vaccine in individuals with egg allergy. Additionally, if influenza vaccine is used in such individuals, the vaccine should be administered by a health-care provider familiar with potential manifestations of egg allergy and recipients should be observed for at least 30 minutes following vaccination. Other measures, such as skin testing or administration of the vaccine in 2 steps (e.g., 10% of the dose initially, followed by remainder of dose if no reaction occurs during 30 minutes of observation), are not necessary in individuals with a history of less severe reactions (i.e., hives only) to eggs. In children who require a second dose of influenza vaccine, use the same product used for the first dose, although a different lot number may be used.

Individuals with a history of severe reaction to eggs, including angioedema, respiratory distress (e.g., wheezing, throat swelling), cardiovascular changes (e.g., hypotension), or GI symptoms (e.g., nausea, vomiting), or any previous reaction requiring epinephrine or other

emergency intervention (particularly reactions that occurred within minutes to hours following egg exposure), should *not* receive influenza vaccine. ACIP and AAP recommend that such individuals be referred to a clinician with expertise in the management of allergic conditions for further risk assessment to determine whether the vaccine should be administered.

Neomycin and/or Polymyxin B Allergy

Afluria[®]: Each 0.5-mL dose may contain trace amounts of neomycin sulfate (≤ 0.2 picograms) and polymyxin B (≤ 0.03 picograms). Manufacturer states the vaccine is contraindicated in individuals hypersensitive to neomycin or polymyxin.

Fluvirin[®]: Each 0.5-mL dose may contain neomycin (≤ 2.5 mcg) and polymyxin B (≤ 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[®], Fluvirin[®]: Some components (i.e., tip cap) 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 or no AIDS-related symptoms. 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⁺ T-cell counts of 400/mm³, the vaccine may be less effective in those with more advanced disease and lower CD4⁺ T-cell counts (e.g., $< 100/\text{mm}^3$). 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.

Fever and Febrile Seizures

Postmarketing reports indicate an increased incidence of fever and febrile seizures in infants and children 6 months through 4 years of age and an increased incidence of fever in children 5–8 years of age who received a 2010 southern hemisphere parenteral inactivated influenza vaccine that is antigenically equivalent to and produced by the same manufacturer as one of the 2010–2011 seasonal parenteral inactivated influenza vaccines marketed in the US (i.e., Afluria[®]; CSL).

In a study evaluating safety and efficacy of the 2009–2010 formulation of Afluria[®], the incidence of fever within 7 days after the first dose was 37% in infants and children 6 months to < 3 years of age, 32% in those 3 to < 5 years of age, and 16% in those 5 to < 9 years of age compared with 14, 11, and 9%, respectively, in children in these age groups who received a comparator vaccine.

Based on available data, ACIP states Afluria[®] should not be used in infants and children 6 months through 8 years of age. (See Pediatric Use under Cautions.)

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[®]: 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[®]: Commercially available in 0.5-mL prefilled syringes as a preservative-free formulation that does not contain thimerosal.

Flulaval[®]: Commercially available in multiple-dose vials containing thimerosal as a preservative (25 mcg of mercury per 0.5 mL).

Fluvirin[®]: 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[®]: 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).

Fluzone[®] Intradermal: Commercially available in 0.1-mL prefilled microinjection systems as a preservative-free formulation.

Fluzone[®] High-Dose: Commercially available in 0.5-mL prefilled syringes as a preservative-free formulation.

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 vaccines are 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 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 vaccines for the 2011–2012 influenza season are expected to provide protection against the 2009 pandemic influenza A (H1N1) virus and influenza A (H3N2) and influenza B viruses represented in the vaccines.

Seasonal influenza vaccines are not expected to provide protection 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 or smaller) to administer the vaccine and apply firm pressure to the injection site (without rubbing) for ≥2 minutes. If patient is receiving antihemophilia or similar 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

Fluarix[®], Flulaval[®], Fluzone[®] Intradermal: Category B.

Afluria[®], Fluvirin[®], Fluzone[®] High-Dose: 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 Congress 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.)

To monitor pregnancy outcomes and newborn health status following influenza vaccination of pregnant women, some manufacturers have established pregnancy registries. Women who receive the vaccine during pregnancy or their healthcare providers may contact the manufacturer at 888-452-9622 (Fluarix[®], Flulaval[®]) or 800-822-2463 (Fluzone[®] Intradermal).

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 influenza vaccination.

Pediatric Use

Flulaval[®], Fluzone[®] Intradermal: Safety and efficacy not established in children <18 years of age.

Fluarix[®]: Safety and efficacy not established in children <3 years of age.

Fluvirin[®]: Safety and efficacy not established in children <4 years of age.

Fluzone[®]: Safety and efficacy not established in infants <6 months of age.

Fluzone[®] High-dose: Safety and efficacy not established in children.

Afluria[®]: Although labeled for use in infants and children ≥5 years of age, ACIP states that Afluria[®] should *not* be used in infants and children 6 months through 8 years of age. Based on available data suggesting Afluria[®] may be associated with increased incidence of fever and febrile seizures in infants and children 6 months through 4 years of age and increased incidence of fever in children 5–8 years of age (see Fever and Febrile Seizures under Cautions), ACIP states that other age-appropriate seasonal influenza vaccines (not Afluria[®]) should be used in infants and children 6 months through 8 years of age. If no other age-appropriate seasonal influenza vaccine is available, ACIP states that Afluria[®] can be used in a child 5–8 years of age who has a medical condition that increases the risk for influenza complications; however, parents or caregivers should be advised of the benefits and risks of vaccination with Afluria[®] before the vaccine is given.

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

Fluzone[®] Intradermal: Safety and efficacy not established in adults ≥65 years of age.

Afluria[®], Fluarix[®], Flulaval[®], Fluvirin[®], Fluzone[®]: No substantial differences in safety relative to younger adults; may be less immunogenic in geriatric individuals.

Fluzone[®] High-Dose: Use *only* in adults ≥65 years of age. Each 0.5 mL of Fluzone[®] High-Dose contains 4 times the amount of antigen contained in Fluzone[®] (see Preparations). Higher incidence of injection site reactions (pain, erythema, swelling) and systemic adverse effects (myalgia, malaise, headache, fever) reported with Fluzone[®] High-Dose compared with Fluzone[®]. There is some evidence that the high-dose formulation elicits higher antibody titers than the standard formulation in adults ≥65 years of age, but additional study needed to determine whether this results in greater protection against influenza illness in this age group.

ACIP states that *all* adults ≥65 years of age should be vaccinated against influenza using an IM inactivated influenza vaccine. ACIP does not express a preference for Fluzone[®] High-Dose or any other IM influenza vaccine in this age group, and states that adults ≥65 years may receive a standard-dose preparation (Afluria[®], Agriflu[®], Fluarix[®], Flulaval[®], Fluvirin[®], Fluzone[®]) or Fluzone[®] High-Dose.

Common Adverse Effects

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

Injection site reactions (i.e., ecchymosis, erythema, induration, swelling, pruritus) occur more frequently with intradermal than IM administration.

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 parenteral vaccine should be administered using a different syringe and different injection site.

Specific Drugs

Drug	Interaction	Comments
Aldesleukin	Possible increased antibody response to influenza vaccine in geriatric adults	
Anticoagulants (e.g., warfarin)	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)
Antiviral agents active against influenza (amantadine, rimantadine, oseltamivir, zanamivir)	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
Aspirin	Possible increased antibody response to influenza vaccine in geriatric adults	
Immune globulin (immune globulin IM [IGIM], immune globulin IV [IGIV]) or specific hyperimmune globulin (hepatitis B immune globulin [HBIG], rabies immune globulin [RIG], tetanus immune globulin [TIG], varicella zoster immune globulin [VZIG])	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 or specific hyperimmune globulin
Immunosuppressive agents (e.g., alkylating agents, antimetabolites, corticosteroids, radiation)	Potential for decreased antibody response Corticosteroid therapy (prednisone or equivalent) in a dosage ≥ 2 mg/kg daily or ≥ 20 mg daily given for ≥ 2 weeks is considered immunosuppressive	Children with malignant neoplasms: Administer influenza vaccine ≥ 3 weeks after chemotherapy is completed and peripheral granulocytes and lymphocyte counts are $>1000/\text{mL}$

		Consider deferring vaccination during short-term, high-dose corticosteroid therapy Parenteral inactivated influenza vaccine may be administered to those receiving long-term immunosuppressive therapy
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 [®] 23): Simultaneous administration with parenteral inactivated influenza vaccine does not interfere with the immune response or increase adverse effects of either vaccine	PPSV23 (Pneumovax [®] 23): May be administered simultaneously with parenteral inactivated influenza vaccine using different syringes and different injection sites PCV (Prevnar [®]): May be administered simultaneously with parenteral inactivated influenza vaccine using different syringes and different injection sites
Rotavirus vaccine (RV)	Concomitant use not studied	May be administered simultaneously with or at any interval before or after parenteral inactivated influenza vaccine
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 ≥ 50 years of age results in antibody responses and adverse effects similar to those reported when the vaccines are administered 4 weeks apart	May be given concurrently (using different syringes and different injection sites) or at any interval before or after zoster vaccine

Stability

Storage

Parenteral

Injectable Suspension, for IM Use

2–8°C; do not freeze. If freezing occurs, discard vaccine.

Return multiple-dose vials to 2–8°C between uses. Manufacturers of Afluria[®] and Flulaval[®] state that multiple-dose vials should be discarded if not used within 28 days after they have been entered.

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.)

Injectable Suspension, for Intradermal Use

2–8°C; do not freeze. If freezing occurs, discard vaccine.

Actions

- Inactivated influenza virus vaccines used for prevention of seasonal influenza are trivalent vaccines containing noninfectious, sterile suspensions of suitably inactivated influenza virus types A and B subunits.
- Seasonal inactivated influenza vaccines commercially available in the US 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).
- Seasonal influenza vaccines are formulated annually to contain antigens representative of the strains of influenza A (H1N1), influenza A (H3N2), and influenza B viruses likely to circulate in the US during the upcoming influenza season. For the 2011–2012 season, the antigenic components recommended by FDA for the US formulation are the same as those recommended by WHO (northern hemisphere).
- The 2011–2012 seasonal parenteral inactivated influenza vaccines for the US contain A/California/7/2009 NYMC X-181, A/California/7/2009 X-179A, or A/Christchurch/16/2010 NIB-74 (H1N1); A/Victoria/210/2009 NYMC X-187 (H3N2) (*A/Perth/16/2009-like*); and B/Brisbane/60/2008. The A/California/7/2009 (H1N1) antigen is derived from the pandemic 2009 influenza A (H1N1) virus. A/Christchurch/16/2010 NIB-74 is an A/California/7/2009-like antigen.
- All 3 antigens contained in 2011–2012 seasonal influenza vaccines are the same as those contained in seasonal influenza vaccines used during the previous influenza season (2010–2011).
- Regardless of manufacturer, all seasonal parenteral inactivated influenza vaccines commercially available in the US contain similar influenza antigens and these seasonal inactivated vaccines are considered antigenically equivalent to the seasonal intranasal live influenza vaccine.
- Influenza vaccines stimulate active immunity to influenza virus strains represented in the vaccines.
- Efficacy of influenza vaccines in preventing seasonal influenza virus infection depends on whether the virus strains represented in the vaccines 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 following IM administration of inactivated vaccine.
- Immune response to IM seasonal influenza vaccine may be lower in geriatric individuals, very young children, or individuals who are immunocompromised or have certain chronic medical conditions.
- In adults 18 through 64 years of age, antibody responses following a dose of Fluzone[®] Intradermal have been noninferior to those following an IM dose of Fluzone[®].
- Seasonal influenza vaccines for the 2011–2012 influenza season are expected to provide protection against the 2009 pandemic influenza A (H1N1) virus and influenza A (H3N2) and influenza B strains represented in the vaccines.

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 represented in the vaccine 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.
- Advise patient and/or patient's parent or guardian that annual vaccination against seasonal influenza is necessary.
- Importance of receiving the 2011–2012 seasonal influenza vaccine, even if the individual received the 2010–2011 seasonal influenza vaccine. Although the 2011–2012 seasonal vaccine contains the same antigens contained in the 2010–2011 seasonal influenza vaccine, the duration of protection is unknown and likely declines over time.
- 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 children ≥9 years of age, but that 2 doses of seasonal influenza vaccine may be necessary in some infants and children 6 months through 8 years of age. (See Pediatric Patients under Dosage and Administration.)
- Importance of informing clinicians of any severe or life-threatening allergies, including severe allergy to eggs, or any history of severe reaction after prior influenza vaccination.
- Importance of informing clinicians of severe or unusual 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://vaers.hhs.gov/index>.

- Importance of informing clinician of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as concomitant illnesses (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 (2011–2012)

Parenteral

Injectable suspension, for IM use

15 mcg hemagglutinin each of A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 per 0.5 mL

Afluria[®], CSL
Biotherapies

Agriflu[®], Novartis
Vaccines

Fluarix[®],
GlaxoSmithKline

Flulaval[®],
GlaxoSmithKline

Fluzone[®], Sanofi Pasteur

15 mcg hemagglutinin each of A/Christchurch/16/2010 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 per 0.5 mL

Fluvirin[®], Novartis
Vaccines

60 mcg hemagglutinin each of A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 per 0.5 mL

Fluzone[®] High-Dose,
Sanofi Pasteur

Injectable suspension, for intradermal use

9 mcg hemagglutinin each of A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 per 0.1 mL

Fluzone[®] Intradermal,
Sanofi Pasteur

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