
Influenza Virus Vaccine Live Intranasal (Seasonal)

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

■ Influenza virus vaccine live intranasal stimulates active immunity to influenza virus infection. There are 2 types of influenza virus vaccines commercially available in the US for prevention of seasonal influenza: influenza virus vaccine inactivated and influenza virus vaccine live intranasal. Seasonal inactivated influenza virus vaccine is a trivalent vaccine containing noninfectious, suitably inactivated influenza virus types A and B subunits and is administered IM; seasonal influenza virus vaccine live intranasal is a trivalent vaccine containing live, attenuated (cold-adapted) influenza virus types A and B and is administered intranasally. For information on the IM seasonal influenza vaccine, see Influenza Virus Vaccine Inactivated (Seasonal) 80:12.

Uses

■ Prevention of Seasonal Influenza A and B Virus Infections

Influenza virus vaccine live intranasal is used in adults 18–49 years of age, adolescents, and children 2 years of age or older to stimulate active immunity to influenza virus strains contained in the vaccine for the prevention of seasonal influenza.

Influenza virus vaccine live intranasal 2009–2010 is a trivalent vaccine formulated to contain antigens representative of the strains of influenza A (H3N2), influenza A (H1N1), and influenza B viruses likely to circulate in the US during the 2009–2010 influenza season. Antigens used in the 2009–2010 live intranasal seasonal influenza vaccine are the same or antigenically equivalent to those used in the 2009–2010 parenteral (IM) inactivated seasonal influenza vaccine. The 2009–2010 influenza virus vaccine live intranasal contains A/South Dakota/6/2007 (H1N1) (*A/Brisbane/59/2007-like*), A/Uruguay/716/2007 (H3N2) (*A/Brisbane/10/2007-like*), and B/Brisbane/60/2008.

Following administration of influenza virus vaccine live intranasal, the vaccine viruses replicate in the nasopharynx epithelial cells to induce protective immunity. Although the vaccine strains contained in the intranasal seasonal influenza vaccine are attenuated live virus reassortants and the strains contained in the parenteral seasonal influenza vaccine are inactivated virus subunits, these vaccines are considered antigenically equivalent. However, data directly comparing efficacy of these vaccines are limited.

The US Public Health Service (USPHS) Advisory Committee on Immunization Practices (ACIP), American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP), and other experts state that live intranasal influenza vaccine can be used instead of parenteral inactivated seasonal vaccine for prevention of seasonal influenza in nonpregnant adults and children 2–49 years of age who do not have underlying medical conditions that put them at higher risk for influenza complications and wish to reduce the likelihood of becoming ill with influenza or of transmitting influenza to others. This includes health-care personnel, household contacts, and other individuals (e.g., day-care providers) who are in close contact with individuals at high risk of influenza complications or in close contact with certain immunocompromised individuals (e.g., those not requiring a protective environment, those with diabetes or human immunodeficiency virus [HIV] infection, asthma patients taking corticosteroids). Possible advantages of the live intranasal vaccine over the inactivated parenteral influenza vaccine in such individuals include its potential to induce a broad mucosal and systemic immune response, ease of administration, and improved acceptance of intranasal rather than IM administration; possible disadvantages include restrictions based on age or medical conditions and the risk that the live vaccine virus could be transmitted from the vaccinee to close contacts who are severely immunocompromised.

Influenza virus vaccine live intranasal should *not* be used in health-care workers, household members, or other individuals who have close contact with severely immunocompromised individuals requiring a protective environment (e.g., hematopoietic stem cell transplant [HSCT] recipients). Parenteral inactivated seasonal influenza vaccine should be used in such individuals.

Safety and efficacy of influenza virus vaccine live intranasal have *not* been established in children younger than 2 years of age or adults 50 years of age or older, and the intranasal formulation currently is *not* considered a substitute for seasonal IM influenza virus vaccine inactivated in these age groups.

Safety of influenza virus vaccine live intranasal has *not* been established in individuals with underlying medical conditions that may predispose them to severe disease following wild-type influenza infection.

During periods when seasonal influenza virus vaccine inactivated vaccine is in short supply, use of seasonal influenza virus vaccine live intranasal is encouraged for eligible individuals. Use of seasonal influenza virus vaccine live intranasal in eligible individuals, including health-care workers, might increase availability of seasonal influenza virus vaccine inactivated for individuals in high-risk groups.

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).

For further information on recommendations for use of seasonal influenza vaccines, including information on choice of influenza vaccines, timing of influenza vaccination, management of influenza exposure (e.g., use of antiviral prophylaxis), and antigenic characteristics of influenza viruses and the choice of antigens for annual formulations of seasonal influenza vaccines, see Influenza Virus Vaccine Inactivated (Seasonal) 80:12.

Information regarding influenza surveillance and updated recommendations for prevention and treatment of seasonal influenza is available from the Centers for Disease Control and Prevention (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>.

Children and Adolescents 2–17 Years of Age

Influenza virus vaccine live intranasal can be used to provide protection against influenza infection in children and adolescents 2–17 years of age. In randomized, placebo-controlled trials in children 6 months of age or older, a protective effect was achieved in about 85–94% of children receiving the vaccine.

Adults 18–49 Years of Age

Influenza virus vaccine live intranasal can be used to provide protection against influenza infection in adults 18–49 years of age. Results of one study in adults 18–46 years of age indicate that administration of intranasal influenza virus vaccine live intranasal is about 57% effective in preventing laboratory-confirmed influenza; this study was carried out during an influenza season when most circulating viruses were not similar to those included in the vaccine.

Travelers

Travelers who want to reduce their risk for influenza infection should consider 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.

Healthy Close Contacts of Individuals with Altered Immunocompetence

Influenza virus vaccine live intranasal should *not* be used in household members, health-care workers, or other individuals who have close contact with severely immunocompromised individuals requiring a protective environment (e.g., HSCT recipients) because of the theoretical risk that the live vaccine virus could be transmitted to these individuals. Therefore, the ACIP states that close contacts of severely immunosuppressed individuals should receive seasonal parenteral influenza virus vaccine inactivated (not influenza virus vaccine live intranasal).

Either seasonal influenza virus vaccine live intranasal or seasonal parenteral influenza virus vaccine inactivated can be used in individuals 2–49 years of age (including health-care workers and employees of long-term care and assisted-living facilities) who have close contact with individuals who are less severely immunocompromised (e.g., those not requiring a protective environment, those with diabetes or HIV infection, asthma patients taking corticosteroids).

Dosage and Administration

■ Administration

Influenza virus vaccine live intranasal is administered intranasally using the prefilled, single-use sprayer supplied by the manufacturer. *The vaccine should not be administered IM, IV, or intradermally.*

Influenza virus vaccine live intranasal should be administered every year prior to exposure to seasonal influenza. The optimal time for annual vaccination against seasonal influenza cannot be determined because influenza seasons vary in their 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. Vaccination efforts should begin each year as soon as the seasonal influenza vaccine is available (usually available beginning in September or October) and continue throughout the 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 influenza A (H1N1)

virus, The US Public Health Service (USPHS) Advisory Committee on Immunization Practices (ACIP) recommends that immunization against seasonal influenza be initiated as soon as the seasonal vaccine is available (e.g., September).

The vaccine recipient should be placed in an upright position with the head tilted back. Approximately one-half the contents of the prefilled, single-use sprayer should be administered into each nostril. The manufacturer's labeling should be consulted for specific information regarding use of the sprayer.

After the vaccine has been administered, the sprayer should be disposed of carefully (i.e., discard using standard procedures for medical waste).

If the vaccine recipient sneezes after receiving a dose of the intranasal vaccine, the dose should *not* be repeated.

Administration of the intranasal vaccine should be deferred if nasal congestion will impede delivery of the vaccine to the nasopharyngeal mucosa; the intranasal vaccine can be administered when symptoms have subsided. Alternatively, the inactivated influenza virus vaccine can be administered IM.

Influenza virus vaccine live intranasal may be given simultaneously with other age-appropriate vaccines during the same health-care visit. However, the ACIP states that simultaneous administration of seasonal influenza virus vaccine live intranasal and influenza A (H1N1) 2009 monovalent vaccine live intranasal is *not* recommended. (See Drug Interactions: Vaccines.)

Personnel Who May Administer Influenza Virus Vaccine Live Intranasal

Influenza virus vaccine live intranasal must be administered by a health-care provider. Although individuals at high-risk of influenza complications (e.g., those with underlying medical conditions, pregnant women, individuals with asthma, individuals 50 years of age or older) may administer influenza virus vaccine live intranasal, the vaccine should *not* be administered by any individual who is severely immunosuppressed. Introduction of very small amounts of vaccine virus into the environment is likely to occur when administering influenza virus vaccine live; the risk of acquiring vaccine virus from the environment is unknown, but presumed to be limited.

■ **Dosage**

Dosing schedule of influenza virus vaccine live intranasal for prevention of seasonal influenza depends on the individual's age and vaccination status.

A single-dose regimen is used in adults and children 9 years of age or older. To promote an adequate antibody response, a 2-dose regimen is used in children 2–8 years of age who have not previously received influenza vaccine.

A single dose consists of the entire contents of the sprayer (0.2 mL).

Adult Dosage

When influenza virus vaccine live intranasal is used for prevention of seasonal influenza in adults 18–49 years of age, the recommended dosage is 0.2 mL (0.1 mL in each nostril) administered as a single dose.

Pediatric Dosage

When influenza virus vaccine live intranasal is used for prevention of seasonal influenza in children 2–8 years of age who have not previously received any type of influenza vaccine, the recommended dosage is two 0.2-mL doses (0.1 mL in each nostril for each dose) of the intranasal vaccine administered at least 1 month apart.

When used for prevention of seasonal influenza in children 2–8 years of age who previously received 2 doses of any influenza vaccine during a single influenza season, the recommended dosage is 0.2 mL (0.1 mL in each nostril) administered as a single dose.

If a child 2–8 years of age received any type of seasonal influenza vaccine for the first time in a previous season and did not receive a second dose within the same season, the ACIP and the American Academy of Pediatrics (AAP) recommend that the child receive 2 doses the following season given at least 4 weeks apart.

When influenza virus vaccine live intranasal is used for prevention of seasonal influenza in children and adolescents 9–17 years of age, the recommended dosage is 0.2 mL (0.1 mL in each nostril) administered as a single dose.

■ **Special Populations**

Geriatric Patients

Influenza virus vaccine live intranasal is *not* indicated in adults 50 years of age or older, including geriatric adults.

Cautions

■ **Contraindications**

History of hypersensitivity (especially anaphylactic reactions) to egg or egg proteins, gentamicin, gelatin, or arginine.

Life-threatening reaction to previous dose of influenza vaccine.

Children and adolescents 2–17 years of age receiving aspirin or aspirin-containing therapy because of an association of Reye's syndrome with aspirin use and wild-type influenza infection.

■ **Warnings/Precautions**

Hypersensitivity Reactions

Hypersensitivity reactions (e.g., anaphylactic reaction, facial edema, urticaria) have been reported after administration of influenza virus vaccine live intranasal.

Seasonal influenza virus vaccine live intranasal is produced using eggs and can contain residual egg protein that may induce immediate hypersensitivity reactions, including anaphylaxis, in individuals with severe egg allergy. The US Public Health Service (USPHS) Advisory Committee on Immunization Practices (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 Cautions: Contraindications.)

Appropriate medical treatment and supervision must be available for immediate use in case an anaphylactic reaction occurs.

Additional vaccine doses should not be administered to any individual who had a life-threatening reaction to a previous dose. (See Cautions: Contraindications.)

Infants Younger than 24 Months of Age

Increased risk of wheezing and hospitalization reported when influenza virus vaccine live intranasal was used in infants younger than 24 months of age; do *not* use in this age group.

In studies in infants, those 6–23 months of age had an increased incidence of wheezing (5.9%) within 42 days of receiving influenza virus vaccine live intranasal relative to the incidence in infants in this age group who received influenza virus vaccine inactivated (3.8%). In addition, an increase in hospitalizations (4.2%) within 180 days of vaccination with the intranasal vaccine was observed in infants 6–23 months of age relative to infants in this age group given influenza virus vaccine inactivated (3.2%). The incidence of wheezing (2.1%) or hospitalizations (2.1%) in children 24–59 months of age given the intranasal vaccine was similar to the incidence in children in this age group given influenza virus vaccine inactivated (2.5% for wheezing and 2.5% for hospitalization).

Individuals with Asthma or Recurrent Wheezing

Individuals with asthma and children younger than 5 years of age with recurrent wheezing or a recent wheezing episode (within the past 12 months) are at increased risk of wheezing after receiving influenza virus vaccine live intranasal; the vaccine should *not* be administered to these individuals unless the possible benefits outweigh the potential risks. (See Pediatric Use under Cautions: Special Populations.)

Influenza virus vaccine live intranasal has not been evaluated to date in individuals with severe asthma or active wheezing, and the vaccine should *not* be administered to such individuals.

Guillain-Barré Syndrome

If Guillain-Barré syndrome (GBS) developed within 6 weeks of a previous influenza vaccination, the manufacturer states that the decision to administer influenza virus vaccine live intranasal should be based on careful consideration of the possible benefits and potential risks.

It is unclear whether influenza vaccination increases the risk of recurrence of GBS. The American Academy of Pediatrics (AAP) states that influenza vaccines should not be used in children who developed GBS within 6 weeks after a dose of any influenza vaccine. The ACIP states that, as a precaution, individuals who are not at high risk for severe influenza complications and who developed GBS within 6 weeks of a previous dose of influenza vaccine generally should avoid influenza vaccination. Although data are limited, ACIP states that use of influenza vaccine can be considered in individuals with a history of GBS who are at high risk for severe complications from influenza.

Individuals with Altered Immunocompetence and Their Close

Contacts

Only limited data are available regarding safety and efficacy of influenza virus vaccine live intranasal in immunocompromised individuals. Possible benefits and potential risks of the vaccine should be carefully considered in such individuals.

Influenza virus vaccine live intranasal has been used in a limited number of HIV-infected adults (asymptomatic or mildly symptomatic) in a clinical study; no serious adverse effects were reported, but efficacy was not evaluated. CDC, National Institutes of Health (NIH), Infectious Diseases Society of America (IDSA), AAP, and other experts state that HIV-infected children, adolescents, and adults should receive annual vaccination against seasonal influenza; however, influenza virus vaccine inactivated (not influenza virus vaccine live intranasal) should be used for prevention of seasonal influenza in HIV-infected individuals.

ACIP states that live viral vaccines (including influenza virus vaccine live intranasal) usually should not be used in immunocompromised individuals, except in certain circumstances. These experts state use of live virus vaccines can be considered in patients with leukemia, lymphoma, or other malignancies if the disease is in remission and chemotherapy was terminated at least 3 months prior to vaccination. (See Drug Interactions: Immunosuppressive Agents.)

Because of possible transmission of live vaccine viruses, influenza virus vaccine live intranasal should *not* be administered to close contacts of severely immunocompromised individuals requiring a protective environment (e.g., hematopoietic stem cell transplant [HSCT] recipients); however, ACIP states that the vaccine may be administered to close contacts of less severely immunocompromised individuals (e.g., those not requiring a protective environment).

In addition, because of possible transmission of live vaccine viruses, ACIP states that health-care workers who have received influenza virus vaccine live intranasal should avoid contact with severely immunocompromised patients requiring a protective

environment (e.g., HSCT recipients) for 7 days after vaccination. Hospital visitors who have received the vaccine should avoid contact with severely immunosuppressed patients for 7 days after vaccination but may visit patients who are not severely immunosuppressed.

Individuals with Medical Conditions that Increase Risk of Influenza Complications

Safety of influenza virus vaccine live intranasal has *not* been established in individuals with underlying medical conditions that increase risk for complications following wild-type influenza infection (e.g., asthma, reactive airway disease, chronic pulmonary or cardiovascular disorders, diabetes, renal impairment, hemoglobinopathies, known or suspected immunodeficiency). (See Warnings/Precautions: Individuals with Altered Immunocompetence and Their Close Contacts under Cautions.) Influenza virus vaccine live intranasal should *not* be administered to these individuals unless the possible benefits outweigh the risks.

Transmission of Vaccine Virus

Intranasal influenza vaccine contains live, attenuated virus. Vaccine virus capable of infection and replication is present in nasal secretions of vaccine recipients, and viral shedding occurs in adults and children who have received the intranasal live vaccine.

Relationship between vaccine virus replication in vaccine recipients and transmission of vaccine virus to other individuals not established. However, transmission of vaccine virus has occurred rarely between vaccine recipients and their contacts.

Duration of vaccine virus replication and shedding in vaccine recipients not established.

Limitations of Vaccine Effectiveness

Up to 2 weeks may be required for protection to develop following seasonal influenza vaccination.

Vaccination with influenza virus vaccine live intranasal may not protect all vaccine recipients from 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. 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.

Influenza virus vaccine live intranasal 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, and is *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. Therefore, annual vaccination is needed for prevention of seasonal influenza.

Vaccine from a previous influenza season should *not* be administered during a subsequent influenza season in an attempt to provide protection.

Concomitant Illness

ACIP states that minor acute illness, such as mild diarrhea or mild upper respiratory tract infection (with or without fever), generally does not preclude vaccination. If nasal congestion will impede delivery of the vaccine to the nasopharyngeal mucosa, influenza virus vaccine live intranasal administration should be deferred until the illness resolves.

Administration Precautions

Health-care personnel who are severely immunosuppressed should *not* administer intranasal live influenza vaccine to patients. (See Personnel Who May Administer Influenza Virus Vaccine Live Intranasal under Dosage and Administration: Administration.) Small amounts of vaccine virus probably are introduced into the environment; the risk of acquiring vaccine virus from the environment is unknown, but presumed to be limited.

Improper Storage and Handling

Seasonal influenza virus vaccine live intranasal should be stored at 2–8°C and should not be frozen. The vaccine does not contain thimerosal or any other preservatives. Improper storage or handling of vaccines may result in loss of vaccine potency and reduced immune response in vaccinees.

All vaccines should be inspected upon delivery and monitored during storage to ensure that the appropriate temperature is maintained.

Influenza virus vaccine live intranasal that has been mishandled or has not been stored at the recommended temperature should not be administered. If there are concerns about mishandling, the manufacturer or state or local health departments should be contacted for guidance on whether the vaccine is usable.

Specific Populations

Pregnancy.

Category C. (See Users Guide.)

Manufacturer states that the vaccine should be used in pregnant women only when clearly needed.

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

Lactation.

Not known whether influenza virus vaccine live intranasal is distributed into milk. Caution is advised if the vaccine is administered in nursing women.

ACIP states that either seasonal influenza virus vaccine live intranasal or seasonal parenteral inactivated influenza vaccine may be used for prevention of seasonal influenza in nursing women, unless contraindicated.

Pediatric Use.

Safety and efficacy of influenza virus vaccine live intranasal established only in children 2 years of age or older.

Do *not* use in infants younger than 24 months of age. Increased incidence of wheezing and hospitalization has been reported in a clinical trial in infants 6–23 months of age† who received intranasal live influenza vaccine compared with those who received parenteral inactivated influenza vaccine. (See Infants Younger than 24 Months of Age under Cautions: Warnings/Precautions.)

Do *not* use in children with asthma or in children younger than 5 years of age with a history of recurrent wheezing or a recent wheezing episode.

When considering use in children 2 through 4 years of age, ACIP and AAP recommend that clinicians screen for possible reactive airways diseases by consulting the child's medical record and asking the child's parent or guardian if wheezing or asthma episodes were identified by a health-care provider within the past 12 months. The seasonal parenteral inactivated influenza vaccine should be used instead of the intranasal live vaccine for prevention of seasonal influenza in such children.

Protection of young infants against seasonal influenza virus depends on immunization of their close contacts. All household contacts, health-care and day-care providers, and other close contacts of young infants should receive seasonal influenza vaccination appropriate for their age and target group.

Adults 50–64 Years of Age.

Influenza virus vaccine live intranasal is *not* indicated for use in adults 50–64 years of age. In a multicenter, placebo-controlled study, the vaccine was not effective in this age group. The seasonal inactivated IM vaccine currently is recommended for prevention of seasonal influenza in this age group.

Geriatric Use.

Influenza virus vaccine live intranasal is *not* indicated for use in geriatric individuals 65 years of age or older. The seasonal inactivated IM vaccine currently is recommended for prevention of seasonal influenza in geriatric adults.

Common Adverse Effects

Adverse effects reported more frequently in adults 18–49 years of age receiving seasonal influenza virus vaccine live intranasal than in those receiving placebo include runny nose (44%), headache (40%), sore throat (28%), tiredness/weakness (26%), muscle aches (17%), cough (14%), chills (9%), nasal congestion (9%), and sinusitis (4%).

Adverse effects reported more frequently in children 2–6 years of age receiving seasonal influenza virus vaccine live intranasal than in those receiving placebo include runny nose/nasal congestion (58%), decreased appetite (21%), irritability (21%), lethargy (14%), sore throat (11%), fever (9%), headache (9%), muscle aches (6%), and chills (4%). Similar adverse effects were reported in older children and adolescents up to 17 years of age; in addition, abdominal pain was reported in 12% and decreased activity reported in 6% of vaccine recipients.

Drug Interactions

Antiviral Agents

Safety and efficacy of concomitant use of seasonal influenza virus vaccine live intranasal with antiviral agents used for treatment or prevention of influenza (e.g., amantadine, rimantadine, oseltamivir, zanamivir) have not been evaluated. Because influenza antiviral agents reduce replication of influenza viruses, these drugs potentially could decrease the immune response to influenza virus vaccine live intranasal.

Influenza virus vaccine live intranasal should not be administered until at least 48 hours after influenza antiviral agent therapy is discontinued and influenza antiviral agents should not be administered until at least 2 weeks after administration of the live vaccine.

If an influenza antiviral agent and influenza virus vaccine live intranasal are administered concomitantly, consider revaccination if appropriate. The US Public Health Service Advisory Committee on Immunization Practices (ACIP) recommends revaccination if an influenza antiviral agent was given 2 days before to 14 days after vaccination.

Aspirin

Influenza virus vaccine live intranasal is contraindicated in children and adolescents 2–17 years of age receiving aspirin or aspirin-containing therapy because of association of Reye's syndrome with aspirin use and wild-type influenza infection.

Blood Products

ACIP states that influenza virus vaccine live intranasal can be administered simultaneously with or at any interval before or after whole blood, packed red blood cells, plasma, and platelet products without substantially decreasing the antibody response to the vaccine.

Immune Globulins

No evidence that 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]) interfere with the immune response to influenza virus vaccine live intranasal. ACIP states that the intranasal live influenza vaccine may be given simultaneously with or at any interval before or after immune globulin preparations.

■ Immunosuppressive Agents

Immunosuppressive agents (e.g., alkylating agents, antimetabolites, corticosteroids, radiation) may decrease the antibody response to influenza virus vaccine live intranasal and may increase the risk of adverse effects. Like other live viral vaccines, influenza virus vaccine live intranasal should not be used in individuals receiving immunosuppressive therapy.

The optimum interval between discontinuance of immunosuppressive therapy and subsequent administration of a live viral vaccine has not been determined.

Live viral vaccines generally are contraindicated in patients receiving high dosages of systemic corticosteroids or when systemic immunosuppression occurs with prolonged topical corticosteroid therapy. Corticosteroid therapy (prednisone or equivalent) in a dosage at least 2 mg/kg daily or at least 20 mg daily given for 2 weeks or longer is considered immunosuppressive, and administration of live viral vaccines should be delayed for at least 1 month after such therapy is discontinued. Short-term (less than 2 weeks), low- to moderate-dose systemic corticosteroid therapy (less than 20 mg of prednisone or equivalent daily); long-term, alternate-day systemic corticosteroid therapy using short-acting drugs; maintenance physiologic doses (replacement therapy); topical corticosteroid therapy (e.g., cutaneous, ophthalmic); corticosteroids given by inhalation; or intra-articular, bursal, or tendon injections of corticosteroids should not be immunosuppressive and do not necessarily contraindicate administration of live viral vaccines.

ACIP recommends that live viral vaccines generally be deferred for at least 3 months after immunosuppressive therapy is discontinued, including chemotherapy or radiation for leukemia, other hematopoietic malignancies, or solid tumors, or after solid organ transplant.

■ Intranasal Preparations

There are no data regarding concomitant administration of influenza virus vaccine live intranasal with other preparations that are administered intranasally.

■ Vaccines

Inactivated Vaccines and Toxoids

Safety and immunogenicity of influenza virus vaccine live intranasal administered concomitantly with inactivated vaccines have not been specifically determined. The manufacturer states that risks versus benefits of concomitant administration of the live influenza vaccine and inactivated vaccines should be considered.

ACIP and AAP state that, in the absence of specific data indicating interference, inactivated vaccines or toxoids can be administered simultaneously with or at any interval before or after seasonal influenza virus vaccine live intranasal.

Live Vaccines

Intranasal influenza vaccine is a live, attenuated virus vaccine. ACIP and AAP state that influenza virus vaccine live intranasal and other live vaccines generally may be administered simultaneously on the same day. However, data are not available regarding concomitant administration of seasonal influenza virus vaccine live intranasal and influenza A (H1N1) monovalent vaccine live intranasal, and ACIP states that these intranasal influenza vaccines should *not* be administered simultaneously.

ACIP states that some oral live vaccines (e.g., rotavirus vaccine live oral, typhoid vaccine live oral) can be administered concomitantly with or at any interval before or after the intranasal live influenza vaccine. However, because of theoretical concerns that the immune response to other live virus vaccines might be impaired if given within 30 days of another live virus vaccine, the ACIP and AAP state that if influenza virus vaccine live intranasal and other live vaccines are not administered on the same day, they should be administered at least 4 weeks apart.

Concomitant administration of influenza virus vaccine live intranasal with measles, mumps, and rubella virus vaccines live (MMR) and monovalent varicella virus vaccine live has been studied in infants 12–15 months of age†. There was no evidence of interference with the immune response to the measles, mumps, rubella, varicella, or influenza antigens, and adverse effects were similar to those reported in other clinical studies evaluating influenza virus vaccine live intranasal. Safety and immunogenicity of concomitant administration of these vaccines have not been evaluated in infants older than 15 months of age.

There is no evidence to date of reduced antibody responses if oral rotavirus vaccine live is administered concomitantly with influenza virus vaccine live intranasal; therefore, rotavirus vaccine may be administered concomitantly with or at any interval before or after the live influenza vaccine.

Description

Influenza virus vaccine live intranasal used for prevention of seasonal influenza is a trivalent vaccine containing live, attenuated (cold-adapted) influenza virus types A and B that stimulates active immunity to influenza virus infection. The seasonal vaccine is prepared by culturing live attenuated influenza virus reassortants in specific pathogen-free eggs. Following administration of influenza virus vaccine intranasal, vaccine virus replicates in cells lining the nasopharynx. The protective mechanism is not completely understood, but may involve both serum and mucosal antibodies.

Seasonal influenza virus vaccine live intranasal 2009–2010 was formulated based on specifications of the US Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC) to contain strains of influenza A and influenza B viruses likely to circulate in the US during the 2009–2010 influenza season. The strains contained in the seasonal intranasal vaccine are the same or antigenically equivalent to the strains used in the seasonal 2009–2010 parenteral (IM) influenza virus vaccine inactivated.

Each 0.2 mL of seasonal influenza virus vaccine live intranasal 2009–2010 contains $10^{6.5-7.5}$ FFU (fluorescent focus units) each of the following live, attenuated influenza virus reassortants: A/South Dakota/6/2007 (H1N1) (*A/Brisbane/59/2007-like*), A/Uruguay/716/2007 (H3N2) (*A/Brisbane/10/2007-like*), and B/Brisbane/60/2008.

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 the 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 influenza virus vaccine live intranasal, 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 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 children 9 years of age or older, but that 2 doses are necessary in children 2–8 years of age who have not previously received 2 doses of any seasonal influenza vaccine during a single influenza season.

Ask patient and/or patient's parent or guardian if vaccinee has a history of asthma or recurrent wheezing or has had a recent wheezing episode (within the past 12 months). Advise patient's parent or guardian that a history of recurrent wheezing may be an asthma equivalent in children younger than 5 years of age. (See Pediatric Use under Cautions.)

Advise patient and/or patient's parent or guardian that seasonal intranasal influenza vaccine is a live, attenuated virus vaccine and that vaccine virus can be transmitted to close contacts. Necessity of vaccine recipient avoiding close contact with severely immunocompromised individuals for 7 days following vaccination. (See Individuals with Altered Immunocompetence and Their Close Contacts under Cautions.)

Importance of informing clinicians of adverse effects. Clinicians or individuals can report any adverse reactions that occur following vaccination to the manufacturer at 877-633-4411 or 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 (i.e., asthma, recurrent wheezing, Guillain-Barré syndrome).

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.)

Overview[®] (see Users Guide). For additional information on this drug until a more detailed monograph is developed and published, the manufacturer's labeling should be consulted. It is essential that the manufacturer's labeling be consulted for more detailed information on usual cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.

Preparations

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

Influenza Virus Vaccine Live Intranasal Trivalent Types A and B (2009–2010)

Nasal Solution

106.5–7.5 FFU (fluorescent focus units) each of A/South Dakota/6/2007 (H1N1) (*A/Brisbane/59/2007-like*), A/Uruguay/716/2007 (H3N2) (*A/Brisbane/10/2007-like*), and B/Brisbane/60/2008 per 0.2 mL

FluMist[®] (preservative-free; available in 0.2-mL prefilled single-use sprayers), MedImmune