HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Influenza A (H1N1) 2009 Monovalent Vaccine safely and effectively. See full prescribing information for Influenza A (H1N1) 2009 Monovalent Vaccine.

Influenza A (H1N1) 2009 Monovalent Vaccine
Manufactured by Sanofi Pasteur Inc.
Suspension for Intramuscular Injection
Initial US Approval: 1980

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	**[9/2009]**
Dosage and Administration (2.2)	**[9/2009]**

----------INDICATIONS AND USAGE----------

Influenza A (H1N1) 2009 Monovalent Vaccine is an inactivated influenza virus vaccine indicated for active immunization of persons 6 months of age and older against influenza disease caused by pandemic (H1N1) 2009 virus. (1)

----------DOSAGE AND ADMINISTRATION----------

Based on currently available information the vaccination regimen is as follows:

Children

- **6 through 35 months of age** (0.25 mL dose, intramuscular injection):
  - Two 0.25 mL doses approximately one month apart. (2.2)
- **36 months through 9 years of age** (0.5 mL dose, intramuscular injection):
  - Two 0.5 mL doses approximately one month apart. (2.2)
- **10 years of age and older**
  - A single 0.5 mL dose, intramuscular injection. (2.2)

Adults

- A single 0.5 mL dose, intramuscular injection. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

Influenza A (H1N1) 2009 Monovalent Vaccine, a sterile suspension for intramuscular injection, is supplied in four presentations:

- Prefilled syringe, 0.25 mL, no preservative; distinguished by a pink syringe plunger rod (3)
- Prefilled syringe, 0.5 mL, no preservative (3)
- Single-dose vial, 0.5 mL, no preservative (3)
- Multi-dose vial, 5 mL, contains thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose contains 25 mcg mercury. (3, 11)

----------CONTRAINDICATIONS----------

- Severe hypersensitivity to egg proteins or any component of the vaccine or life-threatening reactions after previous administration of any influenza vaccine. (4, 11)

----------WARNINGS AND PRECAUTIONS----------

- If Guillain-Barré syndrome (GBS) has occurred within 6 weeks of previous influenza vaccination, the decision to give Influenza A (H1N1) 2009 Monovalent Vaccine should be based on careful consideration of the potential benefits and risks. (5.1)
- Immunocompromised persons may have a reduced immune response to Influenza A (H1N1) 2009 Monovalent Vaccine. (5.2)

----------ADVERSE REACTIONS----------

Adverse reaction information is based on studies conducted with seasonal trivalent Influenza Virus Vaccine.

- Most common (≥10%) local reactions were soreness at injection site, tenderness, pain, and swelling. (6)
- Most common (≥10%) systemic events were malaise, headache, and myalgia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

----------DRUG INTERACTIONS----------

- Do not mix with other vaccines in the same syringe or vial. (7.1)
- Immunosuppressive therapies may reduce the immune response to Influenza A (H1N1) 2009 Monovalent Vaccine. (7.2)

----------USE IN SPECIFIC POPULATIONS----------

Information in this section is based on seasonal trivalent Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc. (Fluzone vaccine).

- Safety and effectiveness of Influenza A (H1N1) 2009 Monovalent Vaccine have not been established in pregnant women or nursing mothers or children <6 months of age. (8.1, 8.3, 8.4)
- Antibody responses to Fluzone vaccine were lower in the geriatric population than in younger adults. (8.5)

See 17 PATIENT_COUNSELING_INFORMATION.

Revised: September 2009

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION:

1. INDICATIONS AND USAGE

Influenza A (H1N1) 2009 Monovalent Vaccine is an inactivated influenza virus vaccine indicated for active immunization of persons 6 months of age and older against influenza disease caused by pandemic (H1N1) 2009 virus.

2. DOSAGE AND ADMINISTRATION

2.1. Preparation for Administration

Inspect Influenza A (H1N1) 2009 Monovalent Vaccine syringes and vials visually for particulate matter and/or discoloration prior to administration. If either of these conditions exist, the vaccine should not be administered.

Shake the syringe and single-dose vials well before administering the vaccine and shake the multi-dose vial each time before withdrawing a dose of vaccine.

2.2. Recommended Dose and Schedule

Clinical studies are ongoing with Influenza A (H1N1) 2009 Monovalent Vaccine to determine the optimal dosage, number of doses and schedule.

Available data show that children 9 years of age and younger are largely serologically naive to the pandemic (H1N1) 2009 virus. (1) Based upon these data Influenza A (H1N1) 2009 Monovalent Vaccine should be administered as follows:

Children

Children 6 through 35 months of age should receive two 0.25 mL intramuscular doses approximately 1 month apart. (1)

Children 36 months through 9 years of age should receive two 0.5 mL intramuscular doses approximately 1 month apart. (1)

Children 10 years of age and older should receive a single 0.5 mL intramuscular dose. (1)

The preferred sites for intramuscular injections are the anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in toddlers and young children.

The vaccine should not be injected into the gluteal region or into areas where there may be a major nerve trunk.

Adults

Persons 18 years of age and older should receive a single 0.5 mL intramuscular dose.

In adults, the preferred site for intramuscular injection is the deltoid muscle.

The vaccine should not be injected into the gluteal region or into areas where there may be a major nerve trunk.

3. DOSAGE FORMS AND STRENGTHS

Influenza A (H1N1) 2009 Monovalent Vaccine is a sterile suspension for intramuscular injection. [See *Description (11)*]

Influenza A (H1N1) 2009 Monovalent Vaccine is supplied in 4 presentations:

1) Prefilled syringe, 0.25 mL, no preservative, for 6 through 35 months of age; distinguished by a pink syringe plunger rod;
2) Prefilled syringe, 0.5 mL, no preservative, for 36 months of age and older;
3) Single-dose vial, 0.5 mL, no preservative, for 36 months of age and older;
4) Multi-dose vial, 5 mL, for 6 months of age and older, contains thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose contains 25 micrograms (mcg) mercury.

4. CONTRAINDICATIONS

Do not administer Influenza A (H1N1) 2009 Monovalent Vaccine to anyone with a known severe hypersensitivity to egg proteins or any component of the vaccine or life-threatening reactions after previous administration of any influenza vaccine. [See *Warnings and Precautions (5) and Description (11)*]

5. WARNINGS AND PRECAUTIONS

5.1. Guillain-Barré Syndrome

Recurrence of Guillain-Barré syndrome (GBS) has been temporally associated with the administration of influenza vaccine. The decision to give Influenza A (H1N1) 2009 Monovalent Vaccine to individuals who have a prior history of Guillain-Barré syndrome should be based on careful consideration of the potential benefits and risks.

5.2. Altered Immunocompetence

If Influenza A (H1N1) 2009 Monovalent Vaccine is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.

5.3. Preventing and Managing Allergic Reaction

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

5.4. Limitations of Vaccine Effectiveness

Vaccination with Influenza A (H1N1) 2009 Monovalent Vaccine may not protect all recipients.

6. ADVERSE REACTIONS

Sanofi Pasteur's Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (Fluzone®) are manufactured by the same process. The following sub-sections

summarize safety data from clinical experience with seasonal trivalent inactivated influenza vaccines, including Fluzone vaccine.

6.1. Clinical Trial Experience

Adverse event information from clinical trials provides the basis for identifying adverse events that appear to be related to vaccine use and for approximating the rates of these events. However, because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trial of another vaccine, and may not reflect the rates observed in practice.

Adults and Geriatrics

In placebo-controlled studies among adults, the most frequent side effect of vaccination is soreness at the vaccination site (affecting 10%–64% of patients) that lasts <2 days, local pain and swelling. These local reactions typically are mild. Fever, malaise, myalgia, and other systemic symptoms can occur following vaccination and most often affect persons who have had no prior exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6–12 hours after vaccination and can persist for 1–2 days. Placebo-controlled trials demonstrate that among older persons and healthy young adults, administration of split-virus influenza vaccine is not associated with higher rates of systemic symptoms (e.g., fever, malaise, myalgia, and headache) when compared with placebo injections. (2)

Children

The 2003-2004 formulation of Fluzone vaccine was studied in 19 children 6 to 23 months of age and in 12 children 24 to 36 months of age, given in 2 doses one month apart. Local reactions and systemic events were solicited for 3 days after each dose. Most local and systemic reactions were mild. The proportions of local and systemic reactions in children were similar to the proportions in adults. No reported local or systemic reaction required a therapeutic intervention other than analgesics. (3)

6.2. Post-Marketing Experience

The following additional events have been reported during post-approval use of Fluzone vaccine. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Blood and Lymphatic System Disorders: Thrombocytopenia, lymphadenopathy

Immune System Disorders: Anaphylaxis, other allergic/hypersensitivity reactions (including urticaria, angioedema)

Nervous System Disorders: GBS, convulsions, myelitis (including encephalomyelitis and transverse myelitis), facial palsy (Bell's palsy), optic neuritis/neuropathy, brachial neuritis, syncope (shortly after vaccination), dizziness, paresthesia

Vascular Disorders: Vasculitis, vasodilation/flushing

Respiratory, Thoracic and Mediastinal Disorders: Dyspnea, pharyngitis, rhinitis

Skin and Subcutaneous Tissue Disorders: Stevens-Johnson syndrome

General Disorders and Administration Site Conditions: Fever, pain, pruritis, asthenia/fatigue, pain in extremities, chest pain

6.3. Other Adverse Events Associated with Influenza Vaccines

Anaphylaxis has been reported after administration of influenza vaccines. Although Influenza A (H1N1) 2009 Monovalent Vaccine contains only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Allergic reactions include hives, angioedema, allergic asthma, and systemic anaphylaxis. [See *Contraindications (4)*]

The 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barré syndrome (GBS). Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. If influenza vaccine does pose a risk, it is probably slightly more than 1 additional case/1 million persons vaccinated.

Neurological disorders temporally associated with influenza vaccination such as encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus neuropathy have been reported.

Microscopic polyangitis (vasculitis) has been reported temporally associated with influenza vaccination.

7. DRUG INTERACTIONS

7.1. Concomitant Administration with Other Vaccines

There are no data on the concomitant administration of Influenza A (H1N1) 2009 Monovalent Vaccine with seasonal trivalent influenza vaccines.

Influenza A (H1N1) 2009 Monovalent Vaccine should not be mixed with any other vaccine in the same syringe or vial.

If Influenza A (H1N1) 2009 Monovalent Vaccine is to be given at the same time as another injectable vaccine(s), the vaccine(s) should always be administered at different injection sites.

7.2. Immunosuppressive Therapies

If Influenza A (H1N1) 2009 Monovalent Vaccine is administered to immunosuppressed persons or persons receiving immunosuppressive therapy, immunologic response may be diminished.

8. USE IN SPECIFIC POPULATIONS

Sanofi Pasteur's Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (Fluzone vaccine) are manufactured by the same process. Available information for Fluzone vaccine is provided in this section.

8.1. Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with Influenza A (H1N1) 2009 Monovalent Vaccine or Fluzone vaccine. It is also not known whether these vaccines can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Influenza A (H1N1) 2009 Monovalent Vaccine should be given to a pregnant woman only if clearly needed.

8.3. Nursing Mothers

It is not known whether Influenza A (H1N1) 2009 Monovalent Vaccine or Fluzone vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this vaccine is administered to a nursing woman.

8.4. Pediatric Use

Safety and effectiveness in pediatric subjects below the age of 6 months have not been established. The immune response and safety of Fluzone vaccine was evaluated in 31 children between the ages of 6-26 months. [See *Adverse Reactions (6.1), Clinical Studies (14)*]

8.5. Geriatric Use

Immune response to Fluzone vaccine in subjects older than 61 years of age were lower when compared to immune responses in adults 19-59 years of age. [See *Clinical Studies (14)*]

11. DESCRIPTION

Influenza A (H1N1) 2009 Monovalent Vaccine, an inactivated influenza virus vaccine, for intramuscular use, is prepared from influenza viruses propagated in embryonated chicken eggs. The virus-containing allantoic fluid is harvested and inactivated with formaldehyde. Influenza virus is concentrated and purified in a linear sucrose density gradient solution using a continuous flow centrifuge. The virus is then chemically disrupted using a non-ionic surfactant, polyethylene glycol p-isooctylphenyl ether (Triton® X-100), producing a "split virus". The split virus is further purified and then suspended in sodium phosphate-buffered isotonic sodium chloride solution.

Influenza A (H1N1) 2009 Monovalent Vaccine is formulated to contain 15 mcg hemagglutinin (HA) of influenza A/California/07/2009 (H1N1) v-like virus per 0.5 mL dose. Gelatin 0.05% is added as a stabilizer. Each 0.5 mL dose may contain residual amounts of formaldehyde (not more than 100 mcg), polyethylene glycol p-isooctylphenyl ether (not more than 0.02%), and sucrose (not more than 2.0%).

There is no thimerosal used in the manufacturing process of the single-dose presentations of Influenza A (H1N1) 2009 Monovalent Vaccine. The multi-dose presentation of Influenza A (H1N1) 2009 Monovalent Vaccine contains thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose of the multidose presentation contains 25 mcg mercury.

Influenza A (H1N1) 2009 Monvalent Vaccine is a sterile clear to a slightly opalescent suspension.

Antibiotics are not used in the manufacture of Influenza A (H1N1) 2009 Monovalent Vaccine.

All presentations of Influenza A (H1N1) 2009 Monovalent Vaccine do not contain latex.

12. CLINICAL PHARMACOLOGY

12.1. Mechanism of Action

Influenza illness and its complications follow infection with influenza viruses. Global surveillance of influenza identifies yearly antigenic variants. For example, since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation. Specific levels of hemagglutinin inhibition (HI) antibody titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza virus infection. In some human studies, antibody titer of ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects. (4) (5)

Antibodies against one influenza virus type or subtype confer limited or no protection against another. Furthermore, antibodies to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Frequent development of antigenic

variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the usual change of one or more new strains in each year's influenza vaccine.

13. NON-CLINICAL TOXICOLOGY

13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

Neither Fluzone vaccine nor Influenza A (H1N1) 2009 Monovalent Vaccine have been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

14. CLINICAL STUDIES

Sanofi Pasteur's Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (Fluzone vaccine) are manufactured by the same process. Data in this section were obtained in clinical studies conducted with Fluzone vaccine.

14.1. Immunogenicity in the Adult and Geriatric Population

In an observational study of the immunogenicity of Fluzone vaccine in a geriatric population (median age: 72.0 range: 61 to 86 years of age) compared with younger adults (median age: 38.0 range: 19 to 59 years of age; racial distribution was 2 Asian, 11 Black, 106 Caucasian, and 2 other; no gender data were available), the following results were obtained using a single-dose of the year 1999–2000 formulation of Fluzone vaccine. (See Table 1.) Antibody levels were obtained on the day of and just prior to vaccination and approximately 21 days after vaccination. (4)

Table 1: Geometric Mean Titer (GMT) and Percentage (%) Achieving an HI Titer ≥1:40 (N = 58-62) in Adults and the Elderly (after vaccination with Fluzone vaccine)

ANTIGEN			PRE-VACCINE GMT	POST-VACCINE GMT (% TITER ≥40)
A (H3N2)	**Cohort 1999**	Young (N = 60)	16.6	53.1 (72)
		Elderly (N = 61)	20.1	58.2 (70)
	Cohort 2000	Young (N = 58)	18.6	72.7 (79)
		Elderly (N = 62)	18.1	49.7 (68)
A (H1N1)	**Cohort 1999**	Young (N = 60)	11.1	35.6 (49)
		Elderly (N = 61)	12.2	26.5 (38)
	Cohort 2000	Young (N = 58)	8.9	35.9 (54)
		Elderly (N = 62)	6.7	16.0 (23)
B	**Cohort 1999**	Young (N = 60)	14.4	41.4 (38)
		Elderly (N = 61)	9.9	19.4 (10)
	Cohort 2000	Young (N = 58)	9.4	21.5 (38)
		Elderly (N = 62)	7.4	9.9 (11)

N = Number of participants

14.2. Immunogenicity in Children

In a study using 2 doses of Fluzone vaccine (2003-2004) in 31 healthy children 6–36 months of age (3 Black, 23 Caucasian, 2 Hispanic, and 3 other; 15 were male and 16 were female), the following immunogenicity results were obtained on day 0 before vaccination and approximately 14 days after dose number 2. (See Table 2.)

Table 2: Geometric Mean Titer (GMT) and Percentage (%) Achieving an HI Titer of ≥ 1:40 in Children (after vaccination with Fluzone vaccine)

ANTIGEN	PRE-VACCINE GMT	POST-DOSE 2 GMT (% TITER ≥40)
A (H3N2)	7.7	52.9 (77.4)
A (H1N1)	6.5	52.9 (77.4)
B	5.2	27.3 (48.4)

15. REFERENCES

1 Centers for Disease Control and Prevention. Serum Cross-Reactive Antibody Response to a Novel Influenza A (H1N1) Virus After Vaccination with Seasonal Influenza Vaccine. MMWR 2009;58(19):521-524.

2 Centers for Disease Control and Prevention. Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2009;58(RR08):1-52.

3 Sanofi Pasteur Inc. Data on file, 071107.

4 Hannoun C et al. Immunogenicity and protective efficacy of influenza vaccination. Virus Res 2004;103:133-138

5 Hobson D, et al. The role of serum hemagglutinin-inhibiting antibody in protection against challenge infection with influenza A2 and B viruses J Hyg Camb 1972;70:767-777.

16. HOW SUPPLIED/STORAGE AND HANDLING

16.1. How Supplied

Single-dose prefilled syringe, without needle, 0.25 mL, package of 10 prefilled syringes per carton – Product No. NDC 49281-650-25.

Single-dose prefilled syringe, without needle, 0.25 mL, package of 25 prefilled syringes per carton – Product No. NDC 49281-650-70.

Single-dose prefilled syringe, without needle, 0.5 mL, package of 10 prefilled syringes per carton – Product No. NDC 49281-650-50.

Single-dose prefilled syringe, without needle, 0.5 mL, package of 25 prefilled syringes per carton – Product No. NDC 49281-650-90.

Single-dose vial, 0.5 mL, package of 10 vials per carton – Product No. NDC 49281-650-10.

Multi-dose vial, 5 mL, one vial per carton. The vial contains ten 0.5 mL doses – Product No. NDC 49281-640-15.

Vial stoppers and syringe plungers do not contain latex.

16.2. Storage and Handling

Store all Influenza A (H1N1) 2009 Monovalent Vaccine presentations refrigerated at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Discard if vaccine has been frozen.

Between uses, return the multi-dose vial to the recommended storage conditions at 2º to 8ºC (35º to 46ºF).

Do not use after the expiration date shown on the label.

17. PATIENT COUNSELING INFORMATION

- Inform vaccine recipients or guardians that Influenza A (H1N1) 2009 Monovalent Vaccine contains killed viruses and cannot cause influenza.
- Inform vaccine recipients or guardians that there are two influenza vaccine formulations for this influenza season, the monovalent vaccine against influenza disease caused by pandemic (H1N1) 2009 virus and seasonal trivalent influenza vaccine.
- Instruct vaccine recipients or guardians to report any severe or unusual adverse reactions to their health care provider.

Product information
as of September 2009.

Manufactured by:

Sanofi Pasteur Inc.

Swiftwater PA 18370 USA

5860-5862