Influenza Virus Vaccine

Fluzone®

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Fluzone® (Influenza Virus Vaccine) safely and effectively. See full prescribing information for Fluzone.

Fluzone® (Influenza Virus Vaccine)
Suspension for Intramuscular Injection
2008-2009 Formula

Initial US Approval: 1980

INDICATIONS AND USAGE
Fluzone is a vaccine indicated for active immunization in persons 6 months of age and older against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. (1)

DOSAGE AND ADMINISTRATION

Children
- 6 through 35 months of age (0.25 mL dose, intramuscular injection):
  - Previously unvaccinated children – should receive two 0.25 mL doses, one on day 1 followed by another 0.25 mL dose at least one month later. (2.2)
  - Previously vaccinated children (ie, received two doses within the same season) should receive only one 0.25 mL dose. (2.2)
- 36 months through 8 years of age (0.5 mL dose, intramuscular injection):
  - Previously unvaccinated children – should receive two 0.5 mL doses, one on day 1 followed by another 0.5 mL dose at least one month later. (2.2)
  - Previously vaccinated children (ie, received two doses within the same season) should receive only one 0.5 mL dose. (2.2)
- 9 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
Fluzone, a sterile suspension for intramuscular injection, is supplied in four presentations:
- Prefilled syringe, 0.25 mL, no preservative, pediatric dose, 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 µg mercury. (3)

Adverse Reactions: Fluzone may cause local reactions including soreness at the injection site, tenderness, pain, and swelling. (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 Fluzone. (7.2)

USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Nursing Mothers
8.3 Pediatric Use
8.4 Geriatric Use

DESCRIPTION
Fluzone is a viral subunit vaccine manufactured by wild-type cells derived from a recombinant adenovirus vector that produces the influenza A (H1N1) and B virus hemagglutinin subunit proteins. (3)

CLINICAL PHARMACOLOGY
12.1 Mechanism of Action

NON-CLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

CLINICAL STUDIES
14.1 Immunogenicity in the Adult and Geriatric Population
14.2 Immunogenicity in Children

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16.1 How Supplied
16.2 Storage and Handling

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Sections or subsections omitted from the full prescribing information are not listed.
1. INDICATIONS AND USAGE

Fluzone® is an inactivated influenza virus vaccine indicated for active immunization in persons 6 months of age and older against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

2. DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Inspect Fluzone vaccine syringes and vials visually for particulate matter and/or discoloration prior to administration. If either of those conditions exists, 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

Children

Children 6 through 35 months of age who have not previously been vaccinated with an influenza vaccine should receive two 0.25 mL doses, one on day 1 followed by another 0.25 mL dose at least 1 month later.¹

Children 6 through 35 months of age who have previously been vaccinated with two doses of any influenza vaccine should receive only one 0.25 mL dose.¹

Children 36 months through 8 years of age who have not previously been vaccinated with influenza vaccine should receive two 0.5 mL doses, one on day 1 followed by another 0.5 mL dose at least 1 month later. Children 36 months through 8 years of age who have been previously vaccinated with two doses of any influenza vaccine should receive only one 0.5 mL dose.¹

Children 9 years of age and older should receive a single 0.5 mL intramuscular dose.¹

There are recommendations available for needle length in different age groups. For needle length, refer to the Advisory Committee on Immunization Practices (ACIP) recommendations.² For children over 36 months, the deltoid muscle should be used; for children 36 months and younger, the anterolateral aspect of the thigh should be used.

Adults

Fluzone vaccine should be administered as a single 0.5 mL intramuscular dose preferably in 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

Fluzone vaccine is a sterile suspension for intramuscular injection. Each 0.25 mL dose of Fluzone vaccine contains a total of 22.5 micrograms (µg) of influenza virus hemagglutinin and each 0.5 mL dose contains a total of 45 µg of influenza virus hemagglutinin from the 3 influenza virus strains in the vaccine. [See Description (11).]

Fluzone vaccine is supplied in 4 presentations:

1) Prefilled syringe, 0.25 mL, no preservative, pediatric dose, 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 µg mercury.

4. CONTRAINDICATIONS

Do not administer Fluzone 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

Recurrent of Guillain-Barré syndrome (GBS) has been temporally associated with the administration of influenza vaccine. Fluzone vaccine should be administered to individuals who have a prior history of Guillain-Barré syndrome only based on careful consideration of the potential benefits and risks.

5.2 Altered Immunocompetence

If Fluzone 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 Fluzone vaccine may not protect all recipients.

6. ADVERSE REACTIONS

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.

6.1 Clinical Trial Experience

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 (eg, 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 (eg, fever, malaise, myalgia, and headache) when compared with placebo injections.¹

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.¹

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
Fluzone vaccine has been standardized according to the US Public Health Service (USPHS) requirements for the 2008-2009 influenza season and is formulated to contain 45 micrograms (μg) hemagglutinin per 0.5 mL dose in the recommended ratio of 15 μg HA of each of the following 3 strains: A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (A/Brisbane/10/2007-like strain) (H3N2), and B/Florida/04/2006. Gelatin 0.05% is added as a stabilizer. Each 0.5 mL dose may contain residual amounts of formaldehyde (not more than 100 μg), polyethylene glycol p-isoctylphenyl ether (not more than 0.02%), and sucrose (not more than 2.0%).

Fluzone vaccine has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.
14. CLINICAL STUDIES

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.

Table 1: Geometric Mean Titer (GMT) and Percentage (%) Achieving an HI Titer ≥1:40 or Greater (N = 58-62) in Adults and the Elderly

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

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

<table>
<thead>
<tr>
<th>ANTIGEN</th>
<th>PRE-VACCINE GMT</th>
<th>POST-DOSE 2 GMT (%) TITER ≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H3N2)</td>
<td>7.7</td>
<td>52.9 (77.4)</td>
</tr>
<tr>
<td>A (H1N1)</td>
<td>6.5</td>
<td>52.9 (77.4)</td>
</tr>
<tr>
<td>B</td>
<td>5.2</td>
<td>27.3 (48.4)</td>
</tr>
</tbody>
</table>

15. REFERENCES

3 Sanofi Pasteur Inc. Data on file, 071107.

16. HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- Latex-free prefilled syringe, without needle, 0.25 mL, package of 10 prefilled syringes per carton – Product No. NDC 49281-008-25.
- Latex-free prefilled syringe, without needle, 0.5 mL, package of 10 prefilled syringes per carton – Product No. NDC 49281-008-50.
- Latex-free single-dose vial, 0.5 mL, package of 10 vials per carton – Product No. NDC 49281-008-10.
- Latex-free multi-dose vial, 5 mL, one vial per carton. The vial contains ten 0.5 mL doses – Product No. NDC 49281-382-15.

16.2 Storage and Handling

Store all Fluzone 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 2° to 8°C (35° to 46°F).

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

17. PATIENT COUNSELING INFORMATION

- Inform the patient or guardian that Fluzone vaccine contains killed viruses and cannot cause influenza. Fluzone vaccine stimulates the immune system to produce antibodies that protect against influenza, but not against other respiratory diseases. Annual vaccination is recommended.
- Vaccine recipients and guardians should be instructed to report any severe or unusual adverse reactions to their health care provider.

Fluzone vaccine is a registered trademark of Sanofi Pasteur Inc.

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

Product information
as of June 2008.