FLUZONE HIGH-DOSE QUADRIVALENT SOUTHERN HEMISPHERE- influenza a virus a/victoria/4897/2022 ivr-238 (h1n1) antigen (formaldehyde inactivated), influenza a virus a/california/122/2022 (a/thailand/8/2022-like virus (h3n2) antigen (formaldehyde inactivated), influenza b virus b/michigan/01/2021 antigen (formaldehyde inactivated), and influenza b virus b/phuket/3073/2013 antigen (formaldehyde inactivated) injection, suspension

Sanofi Pasteur Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fluzone ® High-Dose Quadrivalent Southern Hemisphere safely and effectively. See full prescribing information for Fluzone High-Dose Quadrivalent Southern Hemisphere.

Fluzone High-Dose Quadrivalent (Influenza Vaccine), Suspension, for intramuscular injection
2024 Formula
Initial U.S. Approval: 2019 (Fluzone High-Dose Quadrivalent)

INDICATIONS AND USAGE

Fluzone High-Dose Quadrivalent Southern Hemisphere is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. (1)
Fluzone High-Dose Quadrivalent Southern Hemisphere is approved for use in persons 65 years of age and older. (1)

DOSAGE AND ADMINISTRATION

For intramuscular use only
A single 0.7 mL dose for intramuscular injection in adults 65 years of age and older (2.1)

DOSAGE FORMS AND STRENGTHS

Suspension for injection in prefilled syringe, 0.7 mL (3)

CONTRAINDICATIONS

Severe allergic reaction to any component of the vaccine, including egg protein, or after previous dose of any influenza vaccine (4)

WARNINGS AND PRECAUTIONS

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks following previous influenza vaccination, the decision to give Fluzone High-Dose Quadrivalent Southern Hemisphere should be based on careful consideration of the potential benefits and risks. (5.1)

ADVERSE REACTIONS

In adults ≥65 years of age, the most common (>10%) injection-site reaction was pain (41.3%); the most common solicited systemic adverse reactions were myalgia (22.7%), headache (14.4%) and malaise (13.2%). (6.1)

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 https://vaers.hhs.gov.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 2/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Fluzone® High-Dose Quadrivalent Southern Hemisphere is a vaccine indicated for active immunization for the prevention of influenza caused by influenza A subtype viruses and type B viruses contained in the vaccine.

Fluzone High-Dose Quadrivalent Southern Hemisphere is indicated for use in persons 65 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular use only

2.1 Dose and Schedule

Fluzone High-Dose Quadrivalent Southern Hemisphere should be administered as a single 0.7 mL injection by the intramuscular route in adults 65 years of age and older.

2.2 Administration

Inspect Fluzone High-Dose Quadrivalent Southern Hemisphere visually for particulate matter and/or discoloration prior to administration. If either of these conditions exists the vaccine should not be administered.

Before administering a dose of vaccine, shake the prefilled syringe.

The preferred site for intramuscular injection is the deltoid muscle. The vaccine should not be injected into the

gluteal area or areas where there may be a major nerve trunk.

Do not administer this product intravenously.

Fluzone High-Dose Quadrivalent Southern Hemisphere should not be combined through reconstitution or mixed with any other vaccine.

3 DOSAGE FORMS AND STRENGTHS

Fluzone High-Dose Quadrivalent Southern Hemisphere is a suspension for injection.

Fluzone High-Dose Quadrivalent Southern Hemisphere is supplied in prefilled syringes, 0.7 mL, for adults 65 years of age and older.

4 CONTRAINDICATIONS

A severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine *[see Description (11)]*, including egg protein, or to a previous dose of any influenza vaccine is a contraindication to administration of Fluzone High-Dose Quadrivalent Southern Hemisphere.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks following any previous influenza vaccination, the decision to give Fluzone High-Dose Quadrivalent Southern Hemisphere should be based on careful consideration of the potential benefits and risks.

The 1976 swine influenza vaccine was associated with an elevated risk of GBS. Evidence for a causal relation of GBS with other influenza vaccines is inconclusive; if an excess risk exists, it is probably slightly more than 1 additional case per 1 million persons vaccinated. GBS has also been temporally associated with influenza disease. (See references 1 and 2.)

5.2 Preventing and Managing Allergic Reactions

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

5.3 Altered Immunocompetence

If Fluzone High-Dose Quadrivalent Southern Hemisphere is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be lower than expected.

5.4 Limitations of Vaccine Effectiveness

Vaccination with Fluzone High-Dose Quadrivalent Southern Hemisphere may not protect all recipients.

6 ADVERSE REACTIONS

Fluzone High-Dose Quadrivalent Southern Hemisphere and Fluzone High-Dose Quadrivalent are manufactured using the same process. This section summarizes data obtained from clinical studies with Fluzone High-Dose Quadrivalent.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trial(s) of a vaccine cannot be directly compared to rates in the clinical trial(s) of another vaccine and may not reflect the rates observed in practice. One clinical study has evaluated the safety of Fluzone High-Dose Quadrivalent.

Study 1 (NCT03282240, see https://clinicaltrials.gov) was a randomized, active-controlled, modified double-blind pre-licensure trial conducted in the U.S. The study compared the safety and immunogenicity of Fluzone High-Dose Quadrivalent to those of Fluzone High-Dose (trivalent formulation). The safety analysis set included 1777 Fluzone High-Dose Quadrivalent recipients, 443 Fluzone High-Dose recipients, and 450 investigational Fluzone High-Dose containing the alternate B influenza strain recipients.

The most common reactions occurring after Fluzone High-Dose Quadrivalent administration were injection-site

pain (41.3%), myalgia (22.7%), headache (14.4%), and malaise (13.2%). Onset usually occurred within the first 3 days after vaccination. The majority of solicited reactions resolved within three days of vaccination.

Table 1 displays solicited adverse reactions for Fluzone High-Dose Quadrivalent compared to Fluzone High-Dose reported within 7 days after vaccination and collected using standardized diary cards.

Table 1: Study 1[*]: Frequency of Solicited Injection-Site Systemic Adverse Reactions within 7 Days after Vaccination with Fluzone High-Dose Quadrivalent or Fluzone High-Dose, Adults 65 Years of Age and Older

	Fluzone High-Dose Quadrivalent (N[†]=1761-1768) Percentage		Fluzone High-Dose[‡] (N[†]=885-889) Percentage	
	Any	**Grade 3**	**Any**	**Grade 3**
Local Reactions				
Injection Site Pain[§]	41.3	0.7	36.4	0.2
Injection Site Erythema[¶]	6.2	0.6	5.7	0.2
Injection Site Swelling[¶]	4.9	0.3	4.7	0.1
Injection Site Induration[¶]	3.7	0.2	3.5	0.1
Injection Site Bruising[¶]	1.3	0.0	1.1	0.0
Systemic Reactions				
Myalgia[§]	22.7	0.9	18.9	0.7
Headache[§]	14.4	0.6	13.6	0.4
Malaise[§]	13.2	0.7	13.4	0.4
Shivering[§]	5.4	0.3	4.7	0.3
Fever[#]	0.4	0.2	0.9	0.2

* NCT03282240
† N is the number of vaccinated participants with available data for the events listed
‡ Safety results for the Fluzone High-Dose and investigational Fluzone High-Dose containing the alternate B influenza strain recipients were pooled for the analysis.
§ Grade 3: A type of AE that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.
¶ Grade 3: > 100 mm
# Grade 3: ≥ 102.1°F (39.0°C)

Based on data from Fluzone High-Dose, solicited injection site reactions and systemic adverse reactions were slightly more frequent after vaccination with Fluzone High-Dose compared to a standard-dose vaccine.

Unsolicited non-serious adverse events were reported in 279 (15.7%) recipients in the Fluzone High-Dose Quadrivalent group and 140 (15.7%) recipients in the Fluzone High-Dose group. The most commonly reported unsolicited adverse event was cough.

Within 180 days post-vaccination, 80 (4.5%) Fluzone High-Dose Quadrivalent recipients and 48 (5.4%) Fluzone High-Dose recipients experienced a serious adverse event (SAE). None of the SAEs were assessed as related to the study vaccines.

6.2 Postmarketing Experience

The following additional adverse events have been spontaneously reported during the postmarketing use of Fluzone High-Dose, Fluzone, or Fluzone Quadrivalent and may occur in people receiving Fluzone High-Dose Quadrivalent Southern Hemisphere. 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. Adverse events were included based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Fluzone High-Dose, Fluzone, or Fluzone Quadrivalent.

- *Blood and Lymphatic System Disorders:* Thrombocytopenia, lymphadenopathy
- *Immune System Disorders:* Anaphylaxis, other allergic/hypersensitivity reactions (including urticaria, angioedema)
- *Eye Disorders:* Ocular hyperemia
- *Nervous System Disorders:* Guillain-Barré syndrome (GBS), convulsions, febrile 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, vasodilatation
- *Respiratory, Thoracic and Mediastinal Disorders:* Dyspnea, cough, wheezing, throat tightness,

oropharyngeal pain, and rhinorrhea
- *Gastrointestinal Disorders:* Vomiting
- *Skin and Subcutaneous Tissue Disorders:* Stevens-Johnson syndrome
- *General Disorders and Administration Site Conditions:* pruritus, asthenia/fatigue, chest pain, chills

8 USE IN SPECIFIC POPULATIONS

Fluzone High-Dose Quadrivalent Southern Hemisphere and Fluzone High-Dose Quadrivalent are manufactured using the same process. Data in this section were obtained in studies with Fluzone High-Dose Quadrivalent.

8.1 Pregnancy

Fluzone High-Dose Quadrivalent Southern Hemisphere is not approved for use in persons <65 years of age. There are limited human data on Fluzone High-Dose and no animal data available on Fluzone High-Dose Quadrivalent Southern Hemisphere to establish whether there is a vaccine-associated risk with use of Fluzone High-Dose Quadrivalent in pregnancy.

8.2 Lactation

Fluzone High-Dose Quadrivalent Southern Hemisphere is not approved for use in persons <65 years of age. No human or animal data are available to assess the effects of Fluzone High-Dose Quadrivalent Southern Hemisphere on the breastfed infant or on milk production/excretion.

8.4 Pediatric Use

Safety and effectiveness of Fluzone High-Dose Quadrivalent Southern Hemisphere in children younger than 18 years of age have not been established.

8.5 Geriatric Use

Safety, immunogenicity, and efficacy of Fluzone High-Dose Quadrivalent have been evaluated in adults 65 years of age and older *[see Adverse Reactions (6.1) and Clinical Studies (14)].*

11 DESCRIPTION

Fluzone High-Dose Quadrivalent Southern Hemisphere for intramuscular injection is an inactivated influenza vaccine, 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, octylphenol ethoxylate (Triton® X-100), producing a "split virus." The split virus is further purified and then suspended in sodium phosphate-buffered isotonic sodium chloride solution. The Fluzone High-Dose Quadrivalent Southern Hemisphere process uses an additional concentration factor after the ultrafiltration step in order to obtain a higher hemagglutinin (HA) antigen concentration.

Fluzone High-Dose Quadrivalent Southern Hemisphere suspension for injection is clear and slightly opalescent in color.

Neither antibiotics nor preservative are used in the manufacture of Fluzone High-Dose Quadrivalent Southern Hemisphere.

The Fluzone High-Dose Quadrivalent Southern Hemisphere prefilled syringe presentation is not made with natural rubber latex.

Fluzone High-Dose Quadrivalent Southern Hemisphere is standardized according to United States Public Health Service requirements and is formulated to contain HA of each of the following four influenza strains recommended for the 2024 Southern Hemisphere influenza season: A/Victoria/4897/2022 IVR-238 (H1N1), A/California/122/2022 SAN-022 (A/Thailand/8/2022-like virus) (H3N2), B/Phuket/3073/2013 (B Yamagata lineage) and B/Michigan/01/2021 (a B/Austria/1359417/2021-like virus, B Victoria lineage). The amounts of HA and other ingredients per dose of vaccine are listed in Table 2.

Table 2: Fluzone High-Dose Quadrivalent Southern Hemisphere Ingredients

Ingredient	Quantity (per dose)
	Fluzone High-Dose Quadrivalent Southern Hemisphere 0.7 mL Dose
Active Substance: Split influenza virus, inactivated strains*:	240 mcg HA total
A (H1N1)	60 mcg HA
A (H3N2)	60 mcg HA
B (Victoria Lineage)	60 mcg HA
B (Yamagata Lineage)	60 mcg HA
Other:	
Sodium phosphate-buffered isotonic sodium chloride solution	QS† to appropriate volume
Formaldehyde	≤140 mcg
Octylphenol ethoxylate	≤350 mcg
Gelatin	None
Preservative	None

* per United States Public Health Service (USPHS) requirement
† Quantity sufficient

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Influenza illness and its complications may follow influenza infection. Global surveillance of influenza viruses identifies yearly antigenic variants. Since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation. Specific levels of hemagglutination 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 titers ≥1:40 have been associated with protection from influenza illness in up to 50% of participants. (See references 3 and 4.)

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. Therefore, influenza vaccines are standardized to contain the hemagglutinins of influenza virus strains representing the influenza viruses likely to be circulating during the influenza season in the hemisphere for which the vaccine is intended.

Fluzone High-Dose Quadrivalent Southern Hemisphere stimulates the immune system to produce antibodies that help prevent influenza disease.

13 NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Fluzone High-Dose Quadrivalent Southern Hemisphere has not been evaluated for carcinogenic or mutagenic potential or for impairment of fertility.

14 CLINICAL STUDIES

Fluzone High-Dose Quadrivalent Southern Hemisphere and Fluzone High-Dose Quadrivalent are manufactured using the same process. Data in this section were obtained in studies with Fluzone High-Dose Quadrivalent.

14.1 Immunogenicity of Fluzone High-Dose Quadrivalent in Adults 65 Years of Age and Older

Study 1 (NCT03282240, see http://clinicaltrials.gov) was a randomized, active-controlled, modified double-blind trial in adults 65 years of age and older conducted in the US. The study compared the safety and immunogenicity of Fluzone High-Dose Quadrivalent to those of Fluzone High-Dose. The objective was to demonstrate immunologic non-inferiority of Fluzone High-Dose Quadrivalent to Fluzone High-Dose, as

assessed by HAI geometric mean antibody titers (GMTs) at Day 28 and seroconversion rates, to strains common to formulations of both vaccines, based on pre-specified criteria.

A total of 2670 adults from 65 years of age were randomized (4:1:1) to receive one dose of either Fluzone High-Dose Quadrivalent or one of two formulations of Fluzone High-Dose (one formulation contained a B strain of the Victoria lineage [TIV-HD1] while the other contained a B strain of the Yamagata lineage [TIV-HD2]).

Females accounted for 58.2% of participants in the Fluzone High-Dose Quadrivalent group and 57.4% of participants in the Fluzone High-Dose group (TIV-HD1 and TIV-HD2, pooled). The mean age was 72.9 years (range: 65 through 100 years) in the Fluzone High-Dose Quadrivalent group and the mean age was 73.0 (range: 65 through 95 years) in the Fluzone High-Dose group. The percentage of subjects 75 years of age or older was 35.4% in the Fluzone High-Dose Quadrivalent group and 35.8% in the Fluzone High-Dose group. Most participants were White (91.2% and 89.7%), followed by Black (6.8% and 8.0%), and Hispanic (2.8% and 2.6%) in the Fluzone High-Dose Quadrivalent and Fluzone High-Dose groups, respectively.

The immunogenicity results of Study 1 are summarized in Table 3 and Table 4 below.

Table 3: Study 1*: Post-vaccination HAI Antibody GMTs and Analyses of Non-inferiority of Fluzone High-Dose Quadrivalent Relative to Fluzone High-Dose, Adults 65 Years of Age and Older, Per-Protocol Analysis Set

Influenza Strain	GMT			GMT Ratio	Met Predefined Non-inferiority Criteria†
	QIV-HD N‡=1679-1680	TIV-HD1§ (B1 Victoria) N‡=423	TIV-HD2¶ (B2 Yamagata) N‡=430	QIV-HD over TIV-HD (95% CI)	
A (H1N1)#	312	374		0.83 (0.744; 0.932)	Yes
A (H3N2)#	563	594		0.95 (0.842; 1.066)	Yes
B1 (Victoria)	516	476	--	1.08 (0.958; 1.224)	Yes
B2 (Yamagata)	578	--	580	1.00 (0.881; 1.129)	Yes

* NCT03282240
† Predefined noninferiority criterion for the GMT ratio: the lower limit of the 95% CI of the GMT ratio (QIV-HD divided by TIV-HD) is >0.667
‡ N is the number of vaccinated participants with available data for the immunologic endpoint listed
§ TIV-HD1 contained A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), and B/Brisbane/60/2008 (B1, Victoria lineage)
¶ TIV-HD2 contained A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), and B/Phuket/3073/2013 (B2, Yamagata lineage)
# Pooled TIV-HD group includes subjects vaccinated with either TIV-HD1 or TIV-HD2 for the A strain comparison

Table 4: Study 1*: Seroconversion Rates and Analyses of Non-inferiority of Fluzone High-Dose Quadrivalent Relative to Fluzone High-Dose, Adults 65 Years of Age and Older, Per-Protocol Analysis Set

Influenza Strain	Seroconversion Rates (Percentage)†			Difference of Seroconversion Rates	Met Predefined Non-inferiority Criteria‡
	QIV-HD N§=1668-1669	TIV-HD1¶ (B1 Victoria) N§=420-421	TIV-HD2# (B2 Yamagata) N§=428	QIV-HD minus TIV-HD (95% CI)	

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Influenza Strain	Seroconversion Rates (Percentage)			Difference of Seroconversion Rates	Met Predefined Non-inferiority Criteria
	QIV-HD N =1668-1669	TIV-HD1 (B1 Victoria) N =420-421	TIV-HD2 (B2 Yamagata) N =428	QIV-HD minus TIV-HD (95% CI)	
A (H1N1)Þ	50.4	53.7		-3.27 (-7.37; 0.86)	Yes
A (H3N2)Þ	49.8	50.5		-0.71 (-4.83; 3.42)	Yes
B1 (Victoria)	36.5	39.0	--	-2.41 (-7.66; 2.70)	Yes
B2 (Yamagata)	46.6	--	48.4	-1.75 (-7.04; 3.53)	Yes

* NCT03282240
† Seroconversion Rates: For subjects with a pre-vaccination titer <10 (1/dil), proportion of subjects with a post-vaccination titer ≥40 (1/dil) and for subjects with a pre-vaccination titer ≥10 (1/dil), proportion of subjects with a ≥four-fold increase from pre-vaccination to post-vaccination titer
‡ Predefined noninferiority criterion for seroconversion: the lower limit of the two-sided 95% CI of the difference of the seroconversion rates (QIV-HD minus TIV-HD) is >-10%
§ N is the number of vaccinated participants with available data for the immunologic endpoint listed
¶ TIV-HD1 contained A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), and B/Brisbane/60/2008 (B1, Victoria lineage)
# TIV-HD2 contained A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), and B/Phuket/3073/2013 (B2, Yamagata lineage)
Þ Pooled TIV-HD group includes subjects vaccinated with either TIV-HD1 or TIV-HD2 for the A strain comparison

Fluzone High-Dose Quadrivalent was as immunogenic as Fluzone High-Dose for GMTs and seroconversion rates for the common influenza strains. Fluzone High-Dose Quadrivalent induced a superior immune response, based on a pre-specified superiority criterion, with respect to the additional B strain than the immune response induced by Fluzone High-Dose formulation that did not contain the additional B strain.

14.2 Efficacy of Fluzone High-Dose in Adults 65 Years of Age and Older

The efficacy of Fluzone High-Dose (trivalent formulation) is relevant to Fluzone High-Dose Quadrivalent since both vaccines are manufactured according to the same process and have overlapping compositions.

Study 2 (NCT01427309) was a multi-center, double-blind, post-licensure efficacy trial conducted in the U.S. and Canada in which adults 65 years of age and older were randomized (1:1) to receive either Fluzone High-Dose or Fluzone. The study was conducted over two influenza seasons (2011-2012 and 2012-2013); 53% of participants enrolled in the first year of the study were re-enrolled and re-randomized in the second year. The per-protocol analysis set for efficacy assessments included 15,892 Fluzone High-Dose recipients and 15,911 Fluzone recipients. The majority (67%) of participants in the per-protocol analysis set for efficacy had one or more high-risk chronic comorbid conditions.

In the per-protocol analysis set, females accounted for 57.2% of participants in the Fluzone High-Dose group and 56.1% of participants in the Fluzone group. In both groups, the median age was 72.2 years (range 65 through 100 years). Overall, most participants in the study were White (95%); approximately 4% of study participants were Black, and approximately 6% reported Hispanic ethnicity.

The primary endpoint of the study was the occurrence of laboratory-confirmed influenza (as determined by culture or polymerase chain reaction) caused by any influenza viral type/subtype in association with influenza-like illness (ILI), defined as the occurrence of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature >99.0°F, chills, tiredness, headaches or myalgia. Participants were monitored for the occurrence of a respiratory illness by both active and passive surveillance, starting 2 weeks post-vaccination for approximately 7 months. After an episode of respiratory illness, nasopharyngeal swab samples were collected for analysis; attack rates and vaccine efficacy were calculated (see Table 5).

Table 5: Study 2*: Relative Efficacy Against Laboratory-Confirmed Influenza† Regardless of Similarity to the Vaccine Components, Associated with Influenza-Like Illness‡, Adults 65 Years of Age and Older

	Fluzone High-Dose N[§]=15,892 n[¶] (%)	Fluzone N[§]=15,911 n[¶] (%)	Relative Efficacy % (95% CI)
Any type/subtype[#]	227 (1.43)	300 (1.89)	24.2 (9.7; 36.5)[Þ]
Influenza A	190 (1.20)	249 (1.56)	23.6 (7.4; 37.1)
A (H1N1)	8 (0.05)	9 (0.06)	11.0 (-159.9; 70.1)
A (H3N2)	171 (1.08)	222 (1.40)	22.9 (5.4; 37.2)
Influenza B[ß]	37 (0.23)	51 (0.32)	27.4 (-13.1; 53.8)

Fluzone High-Dose N[§]=15,892 n[¶] (%) | Fluzone N[§]=15,911 n[¶] (%) | Relative Efficacy % (95% CI)

* NCT01427309
† Laboratory-confirmed: culture or polymerase-chain-reaction–confirmed
‡ Occurrence of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature >99.0°F, chills, tiredness, headaches or myalgia
§ N is the number of vaccinated participants in the per-protocol analysis set for efficacy assessments
¶ n is the number of participants with protocol-defined influenza-like illness with laboratory confirmation
# Primary endpoint
Þ The prespecified statistical superiority criterion for the primary endpoint (lower limit of the 2-sided 95% CI of the vaccine efficacy of Fluzone High-Dose relative to Fluzone >9.1%) was met.
ß In the first year of the study the influenza B component of the vaccine and the majority of influenza B cases were of the Victoria lineage; in the second year the influenza B component of the vaccine and the majority of influenza B cases were of the Yamagata lineage

A secondary endpoint of the study was the occurrence of culture-confirmed influenza caused by viral types/subtypes antigenically similar to those contained in the respective annual vaccine formulations in association with a modified CDC-defined ILI, defined as the occurrence of a temperature >99.0°F (>37.2°C) with cough or sore throat. The efficacy of Fluzone High-Dose relative to Fluzone for this endpoint was 51.1% (95% CI: 16.8; 72.0).

15 REFERENCES

1 Lasky T, Terracciano GJ, Magder L, et al. The Guillain-Barré syndrome and the 1992-1993 and 1993-1994 influenza vaccines. N Engl J Med 1998;339:1797-802.
2 Baxter, R, et al. Lack of Association of Guillain-Barré Syndrome with Vaccinations. Clin Infect Dis 2013;57(2):197-204.
3 Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza vaccination. Virus Res 2004;103:133-138.
4 Hobson D, Curry RL, Beare AS, Ward-Gardner A. The role of serum haemagglutination-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, 0.7 mL (NDC 49281-933-88) (not made with natural rubber latex). Supplied as package of 10 (NDC 49281-933-50).

16.2 Storage and Handling

Store Fluzone High-Dose Quadrivalent Southern Hemisphere refrigerated at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Discard if vaccine has been frozen.

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

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Inform the patient or caregiver that Fluzone High-Dose Quadrivalent Southern Hemisphere contains killed viruses and cannot cause influenza.
- Fluzone High-Dose Quadrivalent Southern Hemisphere stimulates the immune system to produce antibodies that help protect against influenza.
- Instruct that annual influenza vaccination is recommended.
- Instruct vaccine recipients and caregivers to report adverse reactions to their healthcare provider and/or to

Vaccine Adverse Event Reporting System (VAERS).
- Give the Vaccine Information Statements to recipients or caregivers, which are required by the National Childhood Vaccine Injury Act of 1986 prior to each immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Fluzone is a registered trademark of Sanofi Pasteur Inc.

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater, PA 18370 USA

Patient Information Sheet
Fluzone® High-Dose Quadrivalent Southern Hemsiphere
Influenza Vaccine

Please read this information sheet before getting Fluzone High-Dose Quadrivalent Southern Hemsiphere vaccine. This summary is not intended to take the place of talking with your healthcare provider. If you have questions or would like more information, please talk with your healthcare provider.

What is Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine?

Fluzone High-Dose Quadrivalent Southern Hemisphere is a vaccine that helps protect against influenza illness (flu) caused by strains circulating in the southern hemisphere.

Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine is for people 65 years of age and older.

Vaccination with Fluzone High-Dose Quadrivalent Southern Hemsiphere vaccine may not protect all people who receive the vaccine.

Who should not get Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine?

You should not get Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine if you:
- ever had a severe allergic reaction to eggs or egg products.
- ever had a severe allergic reaction after getting any flu vaccine.
- are younger than 65 years of age.

Tell your healthcare provider if you have or have had:
- Guillain-Barré syndrome (severe muscle weakness) after getting a flu vaccine.
- problems with your immune system as the immune response may be diminished.

How is Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine given?

Fluzone High-Dose Quadrivalent Southern Hemsphere vaccine is a shot given into the muscle of the arm.

What are the possible side effects of Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine?

The most common side effects of Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine are:
- pain, redness, and swelling where you got the shot
- muscle ache
- tiredness
- headache

These are not all of the possible side effects of Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine. You can ask your healthcare provider for a list of other side effects that is available to healthcare professionals.

Call your healthcare provider for advice about any side effects that concern you. You may report side effects to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or https://vaers.hhs.gov.

Why should I get Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine instead of a standard-dose quadrivalent influenza vaccine?

Among persons 65 years of age and older, Fluzone High-Dose Quadrivalent Southern Hemisphere generated a similar immune response to Fluzone High-Dose and is expected to provide better protection against influenza compared to standard-dose quadrivalent influenza vaccines.

What are the ingredients in Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine?

Fluzone High-Dose Quadrivalent Southern Hemisphere vaccine contains 4 killed flu virus strains. There is no live flu virus in Fluzone High-Dose Quadrivalent Southern Hemsiphere. Fluzone High-Dose Quadrivalent

Southen Hemisphere cannot cause the flu.

Inactive ingredients include formaldehyde and octylphenol ethoxylate.

Manufactured by: Sanofi Pasteur Inc.
Swiftwater, PA 18370 USA

PRINCIPAL DISPLAY PANEL - 0.7 mL Syringe Label

0.7 mL Single-Dose
Influenza Vaccine
Fluzone® High-Dose
Quadrivalent
Southern Hemisphere
2024 Formula
For 65 yrs of age and older
Mfd by: Sanofi Pasteur Inc.

IM only
Rx only

PRINCIPAL DISPLAY PANEL - 0.7 mL Syringe Package

NDC 49281-933-50
2024 Formula

For Intramuscular
Injection Only

10 Single-Dose
Prefilled Syringes
0.7 mL each
Rx only

Influenza Vaccine
Fluzone® High-Dose
Quadrivalent
Southern Hemisphere

FOR ADULTS
65^{+}

SANOFI PASTEUR

FLUZONE HIGH-DOSE QUADRIVALENT SOUTHERN HEMISPHERE

influenza a virus a/victoria/4897/2022 ivr-238 (h1n1) antigen (formaldehyde inactivated), influenza a virus a/california/122/2022 (a/thailand/8/2022-like virus (h3n2) antigen (formaldehyde inactivated), influenza b virus b/michigan/01/2021 antigen (formaldehyde inactivated), and influenza b virus b/phuket/3073/2013 antigen (formaldehyde inactivated) injection, suspension

Product Information			
Product Type	VACCINE	**Item Code (Source)**	NDC:49281-933
Route of Administration	INTRAMUSCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INFLUENZA A VIRUS A/VICTORIA/4897/2022 IVR-238 (H1N1) ANTIGEN (FORMALDEHYDE INACTIVATED) (UNII: AU5C98U4BB) (INFLUENZA A VIRUS A/VICTORIA/4897/2022 IVR-238 (H1N1) HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED) - UNII:C46XJT9FQ9)	INFLUENZA A VIRUS A/VICTORIA/4897/2022 IVR-238 (H1N1) HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED)	60 ug in 0.7 mL
INFLUENZA A VIRUS A/California/122/2022 SAN-022 (H3N2) ANTIGEN (FORMALDEHYDE INACTIVATED) (UNII: N7CB2U8HAC) (INFLUENZA A VIRUS A/California/122/2022 SAN-022 (H3N2) HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED) - UNII:8L9R8S52VV)	INFLUENZA A VIRUS A/California/122/2022 SAN-022 (H3N2) HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED)	60 ug in 0.7 mL
INFLUENZA B VIRUS B/PHUKET/3073/2013 ANTIGEN (FORMALDEHYDE INACTIVATED) (UNII: B93BQX9789) (INFLUENZA B VIRUS B/PHUKET/3073/2013 HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED) - UNII:9HB0XUS9TM)	INFLUENZA B VIRUS B/PHUKET/3073/2013 HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED)	60 ug in 0.7 mL
INFLUENZA B VIRUS B/MICHIGAN/01/2021 ANTIGEN (FORMALDEHYDE INACTIVATED) (UNII: FF9YP4D23C) (INFLUENZA B VIRUS B/MICHIGAN/01/2021 HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED) - UNII:CQV855H5FG)	INFLUENZA B VIRUS B/MICHIGAN/01/2021 HEMAGGLUTININ ANTIGEN (FORMALDEHYDE INACTIVATED)	60 ug in 0.7 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM PHOSPHATE, DIBASIC, ANHYDROUS (UNII: 22ADO53M6F)	
SODIUM PHOSPHATE, MONOBASIC, ANHYDROUS (UNII: KH7I04HPUU)	
WATER (UNII: 059QF0KO0R)	
OCTOXYNOL-9 (UNII: 7JPC6Y25QS)	
FORMALDEHYDE (UNII: 1HG84L3525)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:49281-933-50	10 in 1 PACKAGE		
1	NDC:49281-933-88	0.7 mL in 1 SYRINGE, GLASS; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA103914	02/14/2024	12/31/2024

Labeler - Sanofi Pasteur Inc. (086723285)

Registrant - Sanofi Pasteur Inc. (086723285)

Establishment

Name	Address	ID/FEI	Business Operations
Sanofi Pasteur Inc.		086723285	MANUFACTURE(49281-933)

Revised: 2/2024 Sanofi Pasteur Inc.