FluQuadri

Quadrivalent Influenza Vaccine
Types A and B
2019 - 2020 Formula

FULL PRESCRIBING INFORMATION:
INDICATIONS AND USAGE

FluQuadri™ is an inactivated quadrivalent influenza vaccine indicated for the prevention of influenza disease caused by influenza types A and B viruses contained in the vaccine in children (6 months to 9 years old), adult with high risk factor (>18 years old), and elderly (>60 years old).

COMPOSITION :
Split influenza virus, inactivated strains:30 µg HA total per 0.25 mL dose, contain:
- A/Brisbane/02/2018 (H1N1) pdm09 - like virus (A/Brisbane/02/2018, IVR-190) .....7.5 mcg
- A/Kansas/14/2017 (H3N2) - like virus (A/Kansas/14/2017, X-327) .....7.5 mcg
- B/Colorado/06/2017 - like virus (B/Maryland/15/2016, BX-69A (Victoria Lineage)) .....7.5 mcg
- B/Phuket/3073/2013 - like virus (B/Yamagata/16/88 lineage) .....7.5 mcg

Split influenza virus, inactivated strains:60 µg HA total per 0.5 mL dose, contain:
- A/Brisbane/02/2018 (H1N1) pdm09 - like virus (A/Brisbane/02/2018, IVR-190) .....15 mcg
- A/Kansas/14/2017 (H3N2) - like virus (A/Kansas/14/2017, X-327) .....15 mcg
- B/Colorado/06/2017 - like virus (B/Maryland/15/2016, BX-69A (Victoria Lineage)) .....15 mcg
- B/Phuket/3073/2013 - like virus (B/Yamagata/16/88 lineage) .....15 mcg

This vaccine complies with WHO recommendations (Northern Hemisphere) for 2019 - 2020 season.

DOSAGE AND ADMINISTRATION
• For intramuscular use only
Dose and Schedule
The dose and schedule for FluQuadri are presented in Table 1.
Table 1: Dose and Schedule for FluQuadri

Age	Dose	Schedule
6 months through 35 months	One or two doses[a] , 0.25 mL each	If 2 doses, administer at least 1 month apart
36 months through 8 years	One or two doses[a] , 0.5 mL each	If 2 doses, administer at least 1 month apart
9 years and older	One dose, 0.5 mL	-

[a]1 or 2 doses depends on vaccination history and local or national recommendations
"-" indicates information is not applicable

Administration
Inspect FluQuadri visually for particulate matter and/or discoloration prior to administration. If either of these conditions exist, the vaccine should not be administered.
Before administering a dose of vaccine, shake the prefilled syringe to uniformly distribute the suspension before administering each dose.

Aseptic technique must be used. Use a separate, sterile syringe and needle, or a sterile disposable unit, for each individual patient to prevent disease transmission. Needles should not be recapped and should be disposed of according to biohazard waste guidelines.
The preferred sites for intramuscular injection are the anterolateral aspect of the thigh in infants 6 months through 11 months of age, the anterolateral aspect of the thigh (or the deltoid muscle if muscle mass is adequate) in persons 12 months through 35 months of age, or the deltoid muscle in persons ≥36 months of age. 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, intradermally, or subcutaneously.
FluQuadri vaccine should not be combined through reconstitution or mixed with any other vaccine.

DOSAGE FORMS AND STRENGTHS
FluQuadri is a suspension for injection.

FluQuadri is supplied in 2 presentations (see Table 1 for Dose and Schedule):
1) Prefilled single-dose syringe (pink syringe plunger rod), 0.25 mL, for persons 6 months through 35 months of age.
2) Prefilled single-dose syringe (clear syringe plunger rod), 0.5 mL, for persons 36 months of age and older.

CONTRAINDICATIONS
A severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine [see COMPOSITION], including egg protein, or to a previous dose of any influenza vaccine is a contraindication to administration of FluQuadri.

WARNINGS AND PRECAUTIONS

General
Before administration of FluQuadri, health-care providers should inform the recipient or parent/guardian of the recipient of the benefits and risks immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccines, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the recipient/guardian before immunization.
As with any vaccine, immunization with influenza vaccine may not protect 100% of individuals.
Influenza virus is remarkably unpredictable in that significant antigenic changes may occur from time to time. It is known that FluQuadri, as now constituted, is not effective against all possible strains of influenza virus. Protection is limited to those strains of virus from which the vaccine is prepared or against closely related strains.

Administration Route Related Precaution
Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel. FluQuadri should not be administered into the buttocks.

Febrile or Acute Disease
Persons with serious acute febrile illness usually should not be vaccinated until their symptoms have abated. Those with mild non-serious febrile illness (such as mild upper respiratory tract infections) may be given influenza vaccine.

Hematologic
Because any intramuscular injection can cause injection site hematoma, in persons with any bleeding disorders, such as hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with FluQuadri should not be administered to persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

Guillain-Barré Syndrome
Recurrence of Guillain-Barré syndrome (GBS) has been temporally associated with administration of influenza vaccine. If GBS has occurred within 6 weeks of previous influenza vaccination, the decision to give FluQuadri should be based on careful consideration of the potential benefits and risks.

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

As with all products, epinephrine hydrochloride solution (1:1.000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occcurs. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings including proper airway management. As each dose may contain traces of formaldehyde and Triton®X-100 which are used during vaccine production, caution should be exercised when the vaccine is administered to subjects with hypersensitivity to one of these substances.

Altered Immunocompetence
If FluQuadri is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the expected immune response may not be obtained.

Limitations of Vaccine Effectiveness
Vaccination with FluQuadri may not protect all recipients.

ADVERSE REACTIONS

Clinical Trials Experience
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.

Children 6 Months through 8 Years of Age
In a multi-center study conducted in the US, children 6 months through 35 months of age received one or two 0.25 mL doses of either FluQuadri or one of two formulations of a comparator trivalent influenza vaccine (TIV-1 or TIV-2), and children 3 years through 8 years of age received one or two 0.5 mL doses of either FluQuadri, TIV-1, or TIV-2. Each of the trivalent formulations contained an influenza type B virus that corresponded to one of the two type B viruses in FluQuadri (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). For participants who received two doses, the doses were administered approximately 4 weeks apart. The safety analysis set included 1841 children 6 months through 35 months of age and 2506 children 3 years through 8 years of age.

In children 6 months through 35 months of age, the most common (≥10%) injection-site reactions were pain (57.0%)[a] or tenderness (54.1%)[b] , erythema (37.3%), and swelling (21.6%); the most common solicited systemic adverse reactions were irritability (54.0%)[b], abnormal crying (41.2%)[b], malaise (38.1%)[a], drowsiness (37.7%)[b], appetite loss (32.3%)[b], myalgia (26.7%)[a], vomiting (14.8%)[b], and fever (14.3%). In children 3 years through 8 years of age, the most common (≥10%) injection-site reactions were pain (66.6%), erythema (34.1%), and swelling (24.8%); the most common solicited systemic adverse reactions were myalgia (38.6%), malaise (31.9%), and headache (23.1%).
During the 28 days following vaccination, a total of 16 (0.6%) recipients in the FluQuadri group, 4 (0.5%) recipients in the TIV-1 group, and 4 (0.6%) recipients in the TIV-2 group, experienced at least one SAE; no deaths occurred. Throughout the study period, a total of 41 (1.4%) recipients in the FluQuadri group, 7 (1.0%) recipients in the TIV-1 group, and 14 (1.9%) recipients in the TIV-2 group, experienced at least one SAE. Three SAEs were considered to be possibly related to vaccination: group in a FluQuadri recipient and 2 episodes of febrile seizure, 1 each in a TIV-1 recipient and a TIV-2 recipient. One death occurred in the TIV-1 group (a drowning 43 days post-vaccination).

[a] Assessed in children 24 months through 35 months of age
[b] Assessed in children 6 months through 23 months of age

Table 2: Study 1[a] Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=1223)			TIV-1[c] (B Victoria) (N[e]=310)			TIV-2[d] (B Yamagata) (N[e]=308)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain[h]	57.0	10.2	1.0	52.3	11.5	0.8	50.3	5.4	2.7
-Tenderness[i]	54.1	11.3	1.9	48.4	8.2	1.9	49.7	10.3	0.0
-Erythema	37.3	1.5	0.2	32.9	1.0	0.0	33.3	1.0	0.0
-Swelling	21.6	0.8	0.2	19.7	1.0	0.0	17.3	0.0	0.0
Sytemic adverse reactions									
-Fever (≥100.4°F)[j]	14.3	5.5	2.1	16.0	6.6	1.7	13.0	4.1	2.0
-Malaise[h]	38.1	14.5	4.6	35.2	14.8	4.7	32.4	12.8	6.8
-Myalgia[h]	26.7	6.6	1.9	26.6	9.4	1.6	25.0	6.8	2.7
-Headache[h]	8.9	2.5	0.6	9.4	3.9	0.0	12.2	4.7	0.0
-Irritabillty[i]	54.0	26.4	3.2	52.8	20.1	3.1	53.5	22.9	2.8
-Crying abnormal[i]	41.2	12.3	3.3	36.5	8.2	1.9	29.9	10.4	2.1
-Drowsiness[i]	37.7	8.4	1.3	32.1	3.8	0.6	31.9	5.6	0.7
-Appetite loss[i]	32.3	9.1	1.8	33.3	5.7	1.9	25.0	8.3	0.7
-Vomiting[i]	14.8	6.2	1.0	11.3	4.4	0.6	13.9	6.3	0.0

[a]NCT01240746
[b]The safety analysis set includes all persons who received at least one dose of study vaccine
[c]2010-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
DInvestigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site tenderness: cries and protests when injection-site is touched; Injection-site erythema, Injection-site swelling: ≥2.5 cm to <5 cm; Fever: >101.3°F to ≤ 103.1°F (6 months through 23 months); ≥101.2°F to ≤102.0°F (24 months through 35 months); Malaise, Myalgia, and Headache: some interference with activity; Irritability: requiring increased attention; Crying abnormal: 1 to 3 hours; Drowsiness: not interested in surroundings or did not wake up for a feed/meal; Appetite loss: missed 1 or 2 feeds/meals completely; Vomiting: 2 to 5 episodes per 24 hours
[g]Grade 3 - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site tenderness: cries when injected limb is moved, or the movement of the injected limb is reduced; Injection-site erythema, Injection-site swelling: ≥5 cm; Fever: >103.1°F (6 months through 23 months); ≥102.1ºF (24 months through 35 months); Malaise, Myalgia, and Headache: Significant; prevents daily activity; Irritability: inconsolable; Crying abnormal: >3 hours; Drowsiness: sleeping most of the time or difficult to wake up; Appetite loss: refuses ≥3 feeds/meals or refuses most feeds/meals; Vomiting: ≥6 episodes per 24 hours or requiring parenteral hydration
[h]Assessed in children 24 months through 35 months of age
[i]Assessed in children 6 months through 23 months of age
[j]Fever measured by any route

Table 3: Study 1[a]: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 3 Years Through 8 Years of Age (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=1669)			TIV-1[c] (B Victoria) (N[e]=424)			TIV-2[d] (B Yamagata) (N[e]=413)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	66.6	15.8	2.1	64.6	9.5	2.0	63.8	11.6	2.8
-Erythema	34.1	2.9	1.8	36.8	3.4	1.2	35.2	2.5	1.8
-Swelling	24.8	2.8	1.4	25.4	1.5	1.2	25.9	2.5	1.8
Sytemic adverse reactions									
-Fever (≥100.4°F)[h]	7.0	2.1	2.1	7.1	2.2	1.2	7.6	2.8	0.8
-Headache	23.1	6.8	2.2	21.2	5.1	2.7	24.4	7.5	2.0
-Malaise	31.9	11.2	5.5	32.8	11.4	5.6	33.4	10.8	5.0
-Myalgia	38.6	12.2	3.3	34.1	9.0	2.7	38.4	11.1	2.8

Adults
In a multi-center trial conducted in the US, adults 18 years of age and older received one dose of either FluQuadri or one of two formulations of comparator trivalent influenza vaccine (TIV-1 or TIV-2). Each of the trivalent formulations contained an influenza type B virus that corresponded to one of the two type B viruses in FluQuadri (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). The safety analysis set included 570 recipients, half aged 18-60 years and half aged 61 years or older.

In adults 18 years and older, the most common (≥10%) injection-site reaction was pain (47.4%); the most common solicited systemic adverse reactions were myalgia (23.7%), headache (15.8%), and malaise (10.5%).
In the follow-up period, there were two SAEs, 1 (0.5%) in the FluQuadri group and 1 (0.5%) in the TIV-2 group. No deaths were reported during the trial period.

Table 4: Study 2[a]: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 3 Days After Vaccination in Adults 18 Years of Age and Older (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=190)			TIV-1[c] (B Victoria) (N[e]=190			TIV-2[d] (B Yamagata) (N[e]=190)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	47.4	6.8	0.5	52.1	7.9	0.5	43.2	6.3	0.0
-Erythema	1.1	0.0	0.0	1.6	0.5	0.0	1.6	0.5	0.0
-Swelling	0.5	0.0	0.0	3.2	0.5	0.0	1.1	0.0	0.0
-Induration	0.5	0.0	0.0	1.6	0.5	0.0	0.5	0.0	0.0
-Ecchymosis	0.5	0.0	0.0	0.5	0.0	0.0	0.5	0.0	0.0
Systemic adverse reactions									
-Myalgia	23.7	5.8	0.0	25.3	5.8	0.0	16.8	5.8	0.0
-Haedache	15.8	3.2	0.5	18.4	6.3	0.5	18.0	4.2	0.0
-Malaise	10.5	1.6	1.1	14.7	3.2	1.1	12.1	4.7	0.5
-Shivering	2.6	0.5	0.0	5.3	1.1	0.0	3.2	0.5	0.0
-Fever (100.4°F)[h]	0.0	0.0	0.0	0.5	0.5	0.0	0.5	0.5	0.0

[a]NCT00988143
[b]The safety analysis set includes all persons who received study vaccine
[c]2009-2010 Fluzone TIV containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]2008-2009 Fluzone TIV containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), and B/Florida/04/2006 (Yamagata lineage), licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: Some interference with activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥5.1 to ≤10 cm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, Malaise, and Shivering: some interference with activity
[g]Grade 3 - Injection-site pain: Significant; prevents daily activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: >10 cm; Fever: ≥102.1°F; Myalgia, Headache, Malaise, and Shivering: Significant; prevents daily activity
[h]Fever measured by any route

Geriatric Adults
In a multi-center trial conducted in the US, adults 65 years of age and older received one dose of either FluQuadri , or one of two formulations of comparator trivalent influenza vaccine (TIV-1 or TIV-2). Each of the trivalent formulations contained an influenza type B virus that corresponded to one of the two type B viruses in FluQuadri (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). The safety analysis set included 675 recipients.

In adults 65 years of age and older, the most common (≥10%) injection-site reaction was pain (32.6%); the most common solicited systemic adverse reactions were myalgia (18.3%), headache (13.4%), and malaise (10.7%).

Three SAEs were reported during the follow-up period, 2 (0.9%) in the TIV-1 group and 1 (0.4%) in the TIV-2 group. No deaths were reported during the trial period.

Table 5: Study 3a: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Adults 65 Years of Age and Older (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=225)			TIV-1[c] (B Victoria) (N[e]=225)			TIV-2[d] (B Yamagata) (N[e]=225)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	32.6	1.3	0.9	28.6	2.7	0.0	23.1	0.9	0.0
-Erythema	2.7	0.9	0.0	1.3	0.0	0.0	1.3	0.4	0.0
-Swelling	1.8	0.4	0.0	1.3	0.0	0.0	0.0	0.0	0.0
Sytemic adverse reactions									
-Myalgia	18.3	4.0	0.4	18.3	4.00	0.0	14.2	2.7	0.4
-Headache	13.4	1.3	0.4	11.6	1.3	0.0	11.6	1.8	0.4
-Malaise	10.7	4.5	0.4	6.3	0.4	0.0	11.6	2.7	0.9
-Fever (≥100.4°F)[h]	1.3	0.0	0.4	0.0	0.0	0.0	0.9	0.4	0.4

[a]NCT01218646
[b]The safety analysis set includes all persons who received study vaccine
[c]2010-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]Investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: some interference with activity; Injection-site erythema and Injection-site swelling: ≥5.1 to ≤10 cm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, and Malaise: some interference with activity
[g]Grade 3 - Injection-site pain: Significant; prevents daily activity; Injection-site erythema and Injection-site swelling: >10 cm; Fever: ≥102.1°F; Myalgia, Headache, and Malaise: Significant; prevents daily activity
[h]Fever measured by any route

Reporting adverse reactions
Persons who receive the vaccine and their guardians should be instructed to report any adverse or unusual reaction to their healthcare provider.

Post-Marketing Experience
Currently, there are no post-marketing data available for FluQuadri vaccine.
The following events have been spontaneously reported during the post-approval use of the trivalent formulation of FluQuadri 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 FluQuadri.
• *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, vasodilation/flushing
• *Respiratory, Thoracic and Mediastinal Disorders:* Dyspnea, pharyngitis, rhinitis, cough, wheezing, throat tightness
• *Skin and Subcutaneous Tissue Disorders:* Stevens-Johnson syndrome
• *General Disorders and Administration Site Conditions:* Pruritus, asthenia/fatigue, pain in extremities, chest pain
• *Gastrointestinal Disorders:* Vomiting

DRUG INTERACTIONS
Data evaluating the concomitant administration of FluQuadri with other vaccines are not available.

USE IN SPECIFIC POPULATIONS

Pregnancy
Animal reproduction studies have not been conducted with FluQuadri. It is also not known whether FluQuadri can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

Nursing Mothers
It is not known whether FluQuadri is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when FluQuadri is administered to a nursing woman.

Pediatric Use
Safety and effectiveness of FluQuadri in children below the age of 6 months have not been established. Safety and immunogenicity of FluQuadri was evaluated in children 6 months through 8 years of age. [See ADVERSE REACTIONS and CLINICAL STUDIES.]

Geriatric Use
Safety and immunogenicity of FluQuadri was evaluated in adults 65 years of age and older. [See ADVERSE REACTIONS and CLINICAL STUDIES.] Antibody responses to FluQuadri are lower in persons ≥65 years of age than in younger adults.

DESCRIPTION

FluQuadri (Quadrivalent Influenza Vaccine) 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 FluQuadri process uses an additional concentration factor after the ultrafiltration step in order to obtain a higher hemagglutinin (HA) antigen concentration. Antigens from the four strains included in the vaccine are produced separately and then combined to make the quadrivalent formulation.

FluQuadri suspension for injection is clear and slightly opalescent in color.
Neither antibiotics nor preservative are used in the manufacture of FluQuadri.
The FluQuadri prefilled syringe is not made with natural rubber latex.

FluQuadri is standardized according to United States Public Health Service requirements and is formulated to contain 60 micrograms (mcg) HA per 0.5 mL dose in the recommended ratio of 15 mcg HA of each of the following four influenza strains recommended for the 2019 - 2020 Northern Hemisphere influenza season. The amounts of HA and other ingredients per dose of vaccine are listed in Table.

Ingredient	Quantity (per dose)	
	FluQuadri 0.25 mL Dose	FluQuadri 0.5 mL Dose
Active Substance: Split influenza virus, inactivated strains[a]:	**30 mcg HA total**	**60 mcg HA total**
A/Brisbane/02/2018 (H1N1)pdm09 - like virus (A/Brisbane/02/2018 IVR-190)	7.5 mcg HA	15 mcg HA
A/Kansas/14/2017 (H3N2) - like virus (A/Kansas/14/2017, X-327)	7.5 mcg HA	15 mcg HA
B/Colorado/06/2017 - like virus (B/Maryland/15/2016, BX-69A) (Victoria Lineage)	7.5 mcg HA	15 mcg HA
B/Phuket/3073/2013 - like virus (B/Yamagata/16/88/ lineage)	7.5 mcg HA	15 mcg HA
Other:		
Sodium phosphate-buffered isotonic sodium chloride solution	QS[b] to appropriate volume	QS[b] to appropriate volume
Formaldehyde	≤50 mcg	≤100 mcg
Octylphenol ethoxylate	≤125 mcg	≤250 mcg
Preservative	None	None

[a]per United States Public Health Service (USPHS) requirement
[b]Quantity Sufficient

CLINICAL PHARMACOLOGY
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. Since 2001, two distinct lineages of influenza B (Victoria and Yamagata lineages) have co-circulated worldwide. Protection from influenza virus infection has not been correlated with a specific level of hemagglutination inhibition (HI) antibody titer post-vaccination. However, in some human studies, antibody titers ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects.

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 in the next season.

Annual vaccination with the current vaccine is recommended because immunity during the year after vaccination declines and because circulating strains of influenza virus change from year to year.

NON-CLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
FluQuadri has not been evaluated for carcinogenic or mutagenic potential or for impairment of fertility.

CLINICAL STUDIES
Immunogenicity of FluQuadri in Children 6 Months through 8 Years of Age
In a multi-center study conducted in the US, 1419 children 6 months through 35 months of age and 2101 children 3 years through 8 years of age were included in the per-protocol immunogenicity analysis. Participants received one or two 0.25 mL doses or one or two 0.5 mL doses, respectively of FluQuadri , TIV-1, or TIV-2. For participants who received two doses, the doses were administered approximately 4 weeks apart.

HI antibody geometric mean titers (GMTs) and seroconversion rates 28 days following vaccination with FluQuadri were non-inferior to those following each TIV for all four strains, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of GMTs [FluQuadri divided by pooled TIV for the A strains, or the TIV containing the corresponding B strain] was >0.66 and the lower limit of the 2-sided 95% CI of the difference in seroconversion rates [FluQuadri minus pooled TIV for the A strains, or the TIV containing the corresponding B strain] was >-10%). For strain A/H1N1, the GMT ratio was 1.03 (95% CI: 0.93; 1.14) and the difference of seroconversion rates was 0.9% (95% CI: -0.9%; 3.0%). For strain A/H3N2, the GMT ratio was 0.99 (95% CI: 0.91; 1.08) and the difference of seroconversion rates was 3.8% (95% CI: 1.4%; 6.3%). For strain B/Brisbane/60/2008 (B Victoria), the GMT ratio was 1.34 (95% CI: 1.20; 1.50) and the difference of seroconversion rates was 10.7% (95% CI: 6.4%; 15.1%). For strain B/Florida/04/2006 (B Yamagata), the GMT ratio was 1.06 (95% CI: 0.94; 1.18) and the difference of seroconversion rates was 2.0% (95% CI: -2.2%; 6.4%). Non-inferiority immunogenicity criteria based on HI antibody GMTs and seroconversion rates were also met when age subgroups (6 months to <36 months and 3 years to <9 years) were examined.

In addition, HI antibody GMTs and seroconversion rates following FluQuadri were higher than those following TIV for the B strain not contained in each respective TIV based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of the GMTs [Fluzone Quadrivalent divided by TIV] >1.5 for each B strain in FluQuadri compared with the corresponding B strain not contained in each TIV and the lower limit of the two 2-sided 95% CI of the difference of the seroconversion rates [FluQuadri minus TIV] >10% for each B strain in FluQuadri compared with the corresponding B strain not contained in each TIV).

Immunogenicity of FluQuadri in Adults ≥18 Years of Age
In a multi-center study conducted in the US, 565 adults 18 years of age and older who had received one dose of FluQuadri , TIV-1, or TIV-2 were included in the per-protocol immunogenicity analysis.

HI antibody GMTs 21 days following vaccination with FluQuadri were non-inferior to those following each TIV for all four strains, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of GMTs [FluQuadri divided by pooled TIV for the A strains, or the TIV containing the corresponding B strain] was >2/3). For strain A/H1N1, the GMT ratio was 1.06 (95% CI: 0.87; 1.31), for strain A/H3N2, the GMT ratio was 0.90 (95% CI: 0.70; 1.15), for strain B/Brisbane/60/2008 (B Victoria), the GMT ratio was 0.89 (95% CI: 0.70; 1.12), and for strain B/Florida/04/2006 (B Yamagata), the GMT ratio was 1.15 (95% CI: 0.93; 1.42).

Immunogenicity of FluQuadri in Geriatric Adults ≥65 Years of Age
In a multi-center study conducted in the US, 660 adults 65 years of age and older were included in the per-protocol immunogenicity analysis.

HI antibody GMTs 21 days following vaccination with FluQuadri were non-inferior to those following TIV for all four strains, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of GMTs [FluQuadri divided by pooled TIV for the A strains, or the TIV containing the corresponding B strain] was >0.66). For strain A/H1N1, the GMT ratio was 0.85 (95% CI: 0.67; 1.09), for strain A/H3N2, the GMT ratio was 1.55 (95% CI: 1.25; 1.92), for strain B/Brisbane/60/2008 (B Victoria), the GMT ratio was 1.27 (95% CI: 1.05; 1.55), and for strain B/Florida/04/2006 (B Yamagata), the GMT ratio was 1.11 (95% CI: 0.90; 1.37). Seroconversion rates 21 days following FluQuadri were non-inferior to those following TIV for H3N2, B/Brisbane, and B/Florida, but not for H1N1, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the difference in seroconversion rates [FluQuadri minus pooled TIV for the A strains, or the TIV containing the corresponding B strain] was >-10%). For strain A/H1N1, the difference of seroconversion rates was -3.86% (95% CI: -11.50%; 3.56%), for strain A/H3N2, the difference of seroconversion rates was 9.77% (95% CI: 1.96%; 17.20%), for strain B/Brisbane/60/2008 (B Victoria), the difference of seroconversion rates was 9.91% (95% CI: 1.96%; 17.70%), and for strain B/Florida/04/2006 (B Yamagata), the difference of seroconversion rates was 1.96% (95% CI: -6.73%; 10.60%).

The HI antibody GMT following FluQuadri was higher than that following TIV-1 for B/Florida but not higher than that following TIV-2 for B/Brisbane, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of the GMTs [FluQuadri divided by TIV] >1.5 for each B strain in FluQuadri alent compared with the corresponding B strain not contained in each TIV). The GMT ratio for B/Brisbane was 1.75 (95% CI: 1.43; 2.14). Seroconversion rates following FluQuadri were higher than those following TIV for the B strain not contained in each respective TIV, based on pre-specified criteria (the lower limit of the two 2-sided 95% CI of the difference of the seroconversion rates [FluQuadri minus TIV] >10% for each B strain in FluQuadri compared with the corresponding B strain not contained in each TIV).

PACKAGING
Box, 5 Prefilled syringe @ 0,5 mL (1 dose) - Adult No. Reg.: DKI1616500243B1
Box, 5 Prefilled syringe @ 0,25 mL (1 dose) - Pediatric No. Reg.: DKI1616500243A1

Storage and Shelf Life
Shelf Life: Either "June 30 of the following year of the start of NH season" or "12 months", whichever is less.
Store all FluQuadri presentations 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.

HARUS DENGAN RESEP DOKTER

Imported by:
PT Aventis Pharma
Jakarta – Indonesia

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA 6491, 6492

FluQuadri

Vaksin Influenza Kuadrivalen
Tipe A and B
Formula 2019 - 2020

KOMPOSISI

Dewasa
Senyawa aktif: Split virus influenza , strain inaktif per 0.5 mL :
A/Brisbane/02/2018 (H1N1)pdm09 - like virus (A/Brisbane/02/2018 IVR-190) ..... 15 mcg
A/Kansas/14/2017 (H3N2) - like virus (A/Kansas/14/2017, X-327)…….…..... 15 mcg
B/Colorado/06/2017 - like virus (B/Maryland/15/2016, BX-69A) (Victoria Lineage)..... 15 mcg
B/Phuket/3073/2013 - like virus (B/Yamagata/16/88/ lineage) ..... 15 mcg
Lainnya:
Sodium phosphate-buffered isotonic sodium chloride solution; Formaldehyde; Octylphenol ethoxylate.

Anak-anak
Senyawa aktif: Split virus influenza , strain inaktif per 0.25 mL :
A/Brisbane/02/2018 (H1N1)pdm09 - like virus (A/Brisbane/02/2018 IVR-190) ..... 7.5 mcg
A/Kansas/14/2017 (H3N2) - like virus (A/Kansas/14/2017, X-327) …..... 7.5 mcg
B/Colorado/06/2017 - like virus (B/Maryland/15/2016, BX-69A) (Victoria Lineage).... 7.5 mcg
B/Phuket/3073/2013 - like virus (B/Yamagata/16/88/ lineage) …..... 7.5 mcg
Lainnya:
Sodium phosphate-buffered isotonic sodium chloride solution; Formaldehyde; Octylphenol ethoxylate.

Vaksin sesuai dengan rekomendasi WHO (Northern Hemisphere) untuk musim 2019 - 2020.

INDIKASI DAN PENGGUNAAN

FluQuadriTM adalah vaksin kuadrivalen atau empat strain virus influenza yang sudah dinon-aktifkan yang dapat digunakan sebagai pencegahan terhadap penyakit influenza yang disebabkan oleh virus influenza tipe A dan B yang terkandung di dalam vaksin untuk digunakan bagi anak-anak (usia 6 bulan sampai 9 tahun), individu dewasa dengan faktor risiko tinggi (> 18 tahun), dan kelompok usia lanjut (> 60 tahun).

DOSIS DAN CARA PEMBERIAN

• Hanya untuk penggunaan intramuskular atau suntikan ke dalam jaringan otot.
Dosis dan waktu pemberian
Dosis dan waktu pemberian untuk FluQuadri seperti ditunjukkan pada Tabel 1.
Tabel 1 : Dosis dan waktu pemberian untuk FluQuadri

Usia	Dosis	Jadwal
6 sampai 35 bulan	Satu atau dua dosis[a] , masing-masing 0.25 mL	Jika 2 dosis, lakukan vaksinasi setidaknya berjarak 1 bulan
36 bulan sampai 8 tahun	Satu atau dua dosis[a] , masing-masing 0.5 mL	Jika 2 dosis, lakukan vaksinasi setidaknya berjarak 1 bulan
9 tahun keatas	Satu dosis, 0.5 mL	-

[a]1 atau 2 dosis tergantung dari riwayat vaksinasi dan rekomendasi lokal atau nasional
"-" mengindikasikan bahwa informasi tersebut tidak dapat diaplikasikan

Cara pemberian
Perhatikan FluQuadri secara visual untuk ada tidaknya perubahan partikel dan atau perubahan warna sebelum pemberian vaksin. Jika salah satu dari kondisi tersebut terjadi maka vaksin tidak boleh digunakan.

Sebelum pemberian dosis vaksin, kocok terlebih dahulu alat suntik yang sudah terisi vaksin hingga suspensi vaksin tercampur rata.

Teknik aseptik harus digunakan. Gunakan alat dan jarum suntik yang steril dan terpisah, atau alat suntik sekali pakai yang steril untuk setiap pasien untuk mencegah penularan penyakit. Jarum tidak boleh ditutup kembali dan harus dibuang sesuai dengan pedoman pengelolaan limbah medis.
Tempat yang dianjurkan untuk penyuntikan intramuskular atau di dalam jaringan otot adalah anterolateral atau area depan atau samping dari paha untuk anak usia 6 sampai 11 bulan, area anterolateral pada paha (atau pada deltoid atau bahu jika massa otot sudah memungkinkan) untuk anak usia 12 sampai 35 bulan, atau pada otot deltoid untuk anak usia di atas 36 bulan. Vaksin tidak boleh disuntikkan di area bokong atau area dimana terdapat cabang saraf utama.

Jangan memberikan produk ini melalui pembuluh darah balik, pada jaringan kulit, atau di bawah jaringan kulit.
Vaksin FluQuadri tidak boleh dicampur dengan vaksin lainnya.

KONTRAINDIKASI

Reaksi alergi hebat (anafilaksis seperti gatal, iritasi dan gangguan pernapasan) terhadap salah satu komponen dari vaksin [lihat Komposisi], termasuk diantaranya terhadap protein telur, atau riwayat alergi pada pemberian vaksin influenza sebelumnya merupakan kontraindikasi pemberian FluQuadri.

PERINGATAN DAN PENCEGAHAN

Umum
Sebelum pemberian FluQuadri, praktisi kesehatan harus menginformasikan penerima vaksin atau orangtua/wali dari penerima vaksin mengenai manfaat dan risiko imunisasi, menanyakan mengenai status kesehatan terkini dari penerima vaksin, mengkaji riwayat penerima vaksin mengenai kemungkinan hipersensitivitas terhadap vaksin atau vaksin sejenis, riwayat imunisasi sebelumnya, adanya kontraindikasi terhadap imunisasi dan mematuhi segala peraturan yang berlaku mengenai informasi yang harus diberikan kepada penerima vaksin/walinya sebelum imunisasi.
Sebagaimana dengan vaksin lainnya, imunisasi dengan vaksin influenza mungkin tidak melindungi 100% individu yang menerima vaksin.
Virus influenza sangat tidak terduga dalam hal perubahan antigenik yang signifikan yang dapat terjadi dari waktu ke waktu. Demikian pula halnya dengan FluQuadri, vaksin ini tidak efektif untuk melawan semua kemungkinan strain virus influenza yang ada. Perlindungan terbatas pada strain virus yang terkandung di dalam vaksin.

Rute pemberian terkait tindakan pencegahan
Jangan berikan vaksin secara injeksi intravaskular: mohon pastikan bahwa jarum tidak menembus pembuluh darah. FluQuadri tidak boleh diberikan di bokong.

Demam atau penyakit akut
Individu dengan penyakit demam akut serius biasanya tidak boleh divaksinasi sampai gejalanya mereda. Individu dengan penyakit demam non-serius ringan (seperti infeksi saluran napas atas ringan) boleh diberikan vaksin influenza.

Hematologis
Karena setiap injeksi intramuskular dapat menyebabkan hematoma di tempat injeksi, pada individu dengan kelainan darah, seperti hemofilia atau trombositopenia, atau pada individu yang menjalani terapi antikoagulan, injeksi intramuskular dengan FluQuadri tidak boleh diberikan kepada individu-individu tersebut kecuali jika manfaat yang didapat lebih besar daripada resikonya. Jika diputuskan untuk memberikan produk apapun secara injeksi intramuskular kepada individu dengan kelainan darah tersebut, maka harus diberikan secara hati-hati, dengan langkah-langkah yang diambil untuk menghindari risiko terbentuknya hematoma setelah injeksi.

Guillain-Barre Syndrome

Terjadinya Guillain-Barre syndrome (GBS) atau peradangan akut pada saraf yang dapat menyebabkan kerusakan sel saraf, untuk sementara ini dapat dikaitkan dengan pemberian vaksin influenza. Jika GBS terjadi dalam jangka waktu 6 minggu sejak vaksinasi influenza sebelumnya, keputusan untuk memberikan FluQuadri harus berdasarkan pertimbangan dari keuntungan dan resikonya.

Pencegahan Dan Penanganan Reaksi Alergi
Tindakan medis yang diperlukan dan pengawasan harus tersedia untuk menangani resiko terjadinya reaksi anafilaksis setelah pemberian vaksin.

Sebagaimana dengan produk lainnya, larutan epinefrin hidroklorida (1:1000) dan bahan-bahan lain yang sesuai harus tersedia untuk penggunaan segera jika terjadi kasus anafilaksis atau reaksi hipersensitivitas akut. Praktisi kesehatan harus mengetahui rekomendasi saat ini untuk manajemen awal jika terjadi anafilaksis di luar rumah sakit termasuk manajemen jalan napas yang tepat. Karena setiap dosis mungkin mengandung sisa-sisa formaldehida dan Triton®X-100 yang digunakan selama produksi vaksin, pemberian vaksin harus dilakukan secara hati-hati kepada subyek dengan hipersensitivitas terhadap bahan-bahan tersebut.

Perubahan Kemampuan Untuk Menghasilkan Respon Kekebalan
Jika FluQuadri diberikan kepada individu dengan gangguan sistem kekebalan, termasuk individu yang sedang menerima terapi yang menekan sistem kekebalan tubuh, maka respon kekebalan yang diharapkan mungkin tidak tercapai.

Keterbatasan dari efektivitas vaksin
Proteksi yang didapat dari vaksinasi FluQuadri mungkin tidak sama untuk semua orang.

EFEK SAMPING

Pengalaman studi klinis
Karena studi klinis dilakukan pada kondisi yang beragam, hasil observasi dari satu eksperimen klinis dari suatu vaksin tidak dapat disamaratakan dengan studi klinis dari vaksin lainnya, dan mungkin tidak mencerminkan hasil yang didapat dalam suatu percobaan.

Pada anak usia 6 sampai 35 bulan, reaksi yang paling umum (≥10%) pada tempat penyuntikan adalah rasa nyeri (57.0%)[a] atau 'terasa lunak' (54.1%)b , ruam merah pada kulit (37.3%), dan pembengkakan (21.6%); reaksi yang diperkirakan paling umum adalah iritasi (54.0%)[b], tangisan yang tidak wajar (41.2%)[b], rasa tidak nyaman (38.1%)[a], rasa kantuk (37.7%)[b], menurunnya nafsu makan (32.3%)[b], nyeri otot (26.7%)[a], muntah-muntah (14.8%)[b], dan demam (14.3%). Pada anak usia 3 sampai 8 tahun, reaksi yang paling umum (≥10%) pada lokasi penyuntikan adalah rasa sakit (66.6%), ruam merah pada kulit (34.1%), dan pembengkakan (24.8%); reaksi yang sudah dapat diperkirakan yang paling umum adalah nyeri otot (38.6%), rasa tidak nyaman (31.9%), dan sakit kepala (23.1%).

Tiga kejadian efek samping yang diperkirakan berhubungan dengan vaksinasi: sesak napas pada penerima FluQuadri dan 2 kejadian kejang akibat demam, satu orang dari setiap penerima TIV-1 dan TIV-2. satu kematian terjadi pada kelompok TIV-1 (gagal pernapasan pada 43 hari setelah vaksinasi).

[a]Berdasarkan penilaian pada anak usia 24 sampai 35 bulan
[b]Berdasarkan penilaian pada anak usia 6 sampai 23 bulan

Table 2: Study 1[a] Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=1223)			TIV-1[c] (B Victoria) (N[e]=310)			TIV-2[d] (B Yamagata) (N[e]=308)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain[h]	57.0	10.2	1.0	52.3	11.5	0.8	50.3	5.4	2.7
-Tenderness[i]	54.1	11.3	1.9	48.4	8.2	1.9	49.7	10.3	0.0
-Erythema	37.3	1.5	0.2	32.9	1.0	0.0	33.3	1.0	0.0
-Swelling	21.6	0.8	0.2	19.7	1.0	0.0	17.3	0.0	0.0
Sytemic adverse reactions									
-Fever (≥100.4°F)[j]	14.3	5.5	2.1	16.0	6.6	1.7	13.0	4.1	2.0
-Malaise[h]	38.1	14.5	4.6	35.2	14.8	4.7	32.4	12.8	6.8
-Myalgia[h]	26.7	6.6	1.9	26.6	9.4	1.6	25.0	6.8	2.7
-Headache[h]	8.9	2.5	0.6	9.4	3.9	0.0	12.2	4.7	0.0
-Irritabillty[i]	54.0	26.4	3.2	52.8	20.1	3.1	53.5	22.9	2.8
-Crying abnormal[i]	41.2	12.3	3.3	36.5	8.2	1.9	29.9	10.4	2.1
-Drowsiness[i]	37.7	8.4	1.3	32.1	3.8	0.6	31.9	5.6	0.7
-Appetite loss[i]	32.3	9.1	1.8	33.3	5.7	1.9	25.0	8.3	0.7
-Vomiting[i]	14.8	6.2	1.0	11.3	4.4	0.6	13.9	6.3	0.0

Injection-site adverse reactions: Efek samping di tempat injeksi
Pain: Nyeri
Tenderness: Nyeri Tekan
Erythema: Eritema
Swelling: Bengkak
Systemic adverse reactions: Efek samping sistemik
Fever: Demam
Malaise: Merasa lemah
Myalgia: Nyeri otot
Headache: Sakit kepala
Irritability: Rewel
Crying abnormal: Menangis terus menerus
Drowsiness: Mengantuk
Appetite loss: Hilang nafsu makan
Vomiting: Muntah

[a]NCT01240746
[b]The safety analysis set includes all persons who received at least one dose of study vaccine
[c]2010-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]Investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site tenderness: cries and protests when injection-site is touched; Injection-site erythema, Injection-site swelling: ≥2.5 cm to <5 cm; Fever: >101.3°F to ≤ 103.1°F (6 months through 23 months); ≥101.2°F to ≤102.0°F (24 months through 35 months); Malaise, Myalgia, and Headache: some interference with activity; Irritability: requiring increased attention; Crying abnormal: 1 to 3 hours; Drowsiness: not interested in surroundings or did not wake up for a feed/meal; Appetite loss: missed 1 or 2 feeds/meals completely; Vomiting: 2 to 5 episodes per 24 hours

[g]Grade 3 - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site tenderness: cries when injected limb is moved, or the movement of the injected limb is reduced; Injection-site erythema, Injection-site swelling: ≥5 cm; Fever: >103.1°F (6 months through 23 months); ≥102.1ºF (24 months through 35 months); Malaise, Myalgia, and Headache: Significant; prevents daily activity; Irritability: inconsolable; Crying abnormal: >3 hours; Drowsiness: sleeping most of the time or difficult to wake up; Appetite loss: refuses ≥3 feeds/meals or refuses most feeds/meals; Vomiting: ≥6 episodes per 24 hours or requiring parenteral hydration
[h]Assessed in children 24 months through 35 months of age
[i]Assessed in children 6 months through 23 months of age
Fever measured by any route

Table 3: Study 1[a]: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 3 Years Through 8 Years of Age (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=1669)			TIV-1[c] (B Victoria) (N[e]=424)			TIV-2[d] (B Yamagata) (N[e]=413)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	66.6	15.8	2.1	63.8	9.5	2.0	63.8	11.6	2.8
-Erythema	34.1	2.9	1.8	35.2	3.4	1.2	35.2	2.5	1.8
-Swelling	24.8	2.8	1.4	25.4	1.5	1.2	25.9	2.5	1.8
Sytemic adverse reactions									
-Fever (100.4°F)[h]	7.0	2.1	2.1	7.1	2.2	1.2	7.6	2.8	0.8
-Headache	23.1	6.8	2.2	21.2	5.1	2.7	24.4	7.5	2.0
-Malaise	31.9	11.2	5.5	32.8	11.4	5.6	33.4	10.8	5.0
-Myalgia	38.6	12.2	3.3	34.1	9.0	2.7	38.4	11.1	2.8

[a]NCT01240746
[b]The safety analysis set includes all persons who received at least one dose of study vaccine
[c]2012-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]Investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N3), and B/Florida/04/2006 (Yamagata lineage), licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site erythema, Injection-site swelling: ≥2.5 cm to <5 cm; Fever: ≥ 101.2°F to ≤102.0°F; Headache, Malaise, and Myalgia: some interference with activity
[g]Grade 3 - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site erythema, Injection-site swelling: ≥5 cm; Fever: ≥102.1°F; Headache, Malaise, and Myalgia: Significant; prevents daily activity
[h]Fever measured by any route

Dewasa
Dari studi multi-senter di Amerika Serikat, pada orang dewasa usia 18 tahun ke atas, reaksi yang paling umum (≥10%) pada tempat penyuntikan adalah rasa nyeri (47.4%), reaksi yang diperkirakan paling umum adalah nyeri otot (23.7%), sakit kepala(15.8%), dan rasa tidak nyaman (10.5%).
Pada masa tindak lanjut pelaporan efek samping, terdapat dua efek samping serius (SAE), satu (0.5%) pada kelompok FluQuadri dan satu (0.5%) pada kelompok TIV-2. Tidak ada kematian yang dilaporkan terjadi selama masa studi klinis.

Table 4: Study 2[a]: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 3 Days After Vaccination in Adults 18 Years of Age and Older (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=190)			TIV-1[c] (B Victoria) (N[e]=190)			TIV-2[d] (B Yamagata) (N[e]=190)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	47.4	6.8	0.5	52.1	7.9	0.5	43.2	6.3	0.0
-Erythema	1.1	0.0	0.0	1.6	0.5	0.0	1.6	0.5	0.0
-Swelling	0.5	0.0	0.0	3.2	0.5	0.0	1.1	0.0	0.0
-Induration	0.5	0.0	0.0	1.6	0.5	0.0	0.5	0.0	0.0
-Ecchymosis	0.5	0.0	0.0	0.5	0.0	0.0	0.5	0.0	0.0
Sytemic adverse reactions									
-Myalgia	23.7	5.8	0.0	25.3	5.8	0.0	16.8	5.8	0.0
-Headache	15.8	3.2	0.5	18.4	6.3	0.5	18.0	4.2	0.0
-Malaise	10.5	1.6	1.1	14.7	3.2	1.1	12.1	4.7	0.5
-Shivering	2.6	0.5	0.0	5.3	1.1	0.0	3.2	0.5	0.0
-Fever (100.4°F)[h]	0.0	0.0	0.0	0.5	0.0	0.0	0.5	0.5	0.0

[a]NCT00988143
[b]The safety analysis set includes all persons who received study vaccine
[c]2009-2010 Fluzone TIV containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]2008-2009 Fluzone TIV containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), and B/Florida/04/2006 (Yamagata lineage), licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: Some interference with activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥5.1 to ≤ 10 cm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, Malaise, and Shivering: some interference with activity
[g]Grade 3 - Injection-site pain: Significant; prevents daily activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: >10 cm; Fever: ≥102.1°F; Myalgia, Headache, Malaise, and Shivering: Significant; prevents daily activity
[h]Fever measured by any route

Tabel 4: (mohon merujuk ke terjemahan di Tabel 2)
Induration: Pengerasan pada kulit
Ecchymosis: Ekimosis / memar
Shivering: Menggigil

Pasien lanjut usia
Pada manula usia 65 tahun ke atas, reaksi yang paling umum (≥10%) pada tempat penyuntikan adalah rasa sakit (32.6%); reaksi yang diperkirakan paling umum adalah nyeri otot (18.3%), sakit kepala (13.4%), dan rasa tidak nyaman (10.7%).
Tiga kejadian efek samping yang dilaporkan selama masa pengawasan setelah masa studi klinis, 2 (0.9%) dari kelompok TIV-1 dan 1 (0.4%) dari kelompok TIV-2. Tidak ada kematian yang dilaporkan terjadi selama masa studi klinis

Table 5: Study 3a: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Adults 65 Years of Age and Older (Safety Analysis Set)[b]

	Fluzone Quadrivalent (N[e]=225)			TIV-1[c] (B Victoria) (N[e]=225)			TIV-2[d] (B Yamagata) (N[e]=225)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
-Pain	32.6	1.3	0.9	28.6	2.7	0.0	23.1	0.9	0.0
-Erythema	2.7	0.9	0.0	1.3	0.0	0.0	1.3	0.4	0.0
-Swelling	1.8	0.4	0.0	1.3	0.0	0.0	0.0	0.0	0.0
Sytemic adverse reactions									
-Myalgia	18.3	4.0	0.4	18.3	4.0	0.0	14.2	2.7	0.4
-Headache	13.4	1.3	0.4	11.6	1.3	0.0	11.6	1.8	0.4
-Malaise	10.7	4.5	0.4	6.3	0.4	0.0	11.6	2.7	0.9
-Fever (100.4°F)[h]	1.3	0.0	0.4	0.0	0.0	0.0	0.9	0.4	0.4

[a]NCT01218646
[b]The safety analysis set includes all persons who received study vaccine
[c]2010-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed
[d]Investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed
[e]N is the number of participants in the safety analysis set
[f]Grade 2 - Injection-site pain: some interference with activity; Injection-site erythema and Injection-site swelling: ≥5.1 to ≤10 cm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, and Malaise: some interference with activity
[g]Grade 3 - Injection-site pain: Significant; prevents daily activity; Injection-site erythema and Injection-site swelling: >10 cm; Fever: ≥102.1°F; Myalgia, Headache, and Malaise: Significant; prevents daily activity
[h]Fever measured by any route

Tabel 5: (Mohon merujuk ke terjemahan di tabel-tabel sebelumnya)

Laporan mengenai reaksi yang tidak diinginkan
Para penerima vaksin dan para pengawasnya diharapkan melaporkan segala bentuk efek samping atau reaksi yang tidak diinginkan kepada penyedia layanan kesehatan mereka.

Kejadian pasca pemasaran
Sampai saat ini, tidak ada data pasca pemasaran yang tersedia untuk vaksin FluQuadri Kejadian berikut ini secara spontan dilaporkan selama masa penggunaan FluQuadri yang sudah disetujui. Karena kejadian berikut ini dilaporkan secara sukarela oleh populasi dari beragam usia, maka tidak dapat secara akurat menentukan estimasi dari frekuensi kejadian yang disebabkan dari paparan vaksin. Kejadian pertentangan yang terjadi didasarkan dari beberapa faktor berikut: keparahan, frekuensi terjadinya, atau kuatnya bukti hubungan sebab akibat terhadap FluQuadri.
- *Kelainan pada darah dan jaringan getah bening:* Trombositopenia, Limfadenopati
- *Kelainan sistem kekebalan tubuh:* anafilaksis, reaksi alergi atau hipersensitif lainnya (termasuk urtikaria angioedema)
- *Kelainan mata:* Mata merah
- *Kelainan pada sistem saraf:* Guillain-Barre Syndrome (GBS), kejang, kejang demam, mielitis (termasuk ensefalomielitis dan myelitis transversa), kelumpuhan pada wajah (Bell's palsy), kerusakan saraf pada area mata/neuropati, neuritis pada area lengan, pingsan (sesaat setelah vaksinasi), rasa pusing, kesemutan.
- *Kelainan pada pembuluh darah:* vaskulitis, pelebaran pembuluh darah.
- *Kelainan pernapasan, dada dan rongga dada:* kesulitan bernapas, radang tenggorokan, radang pada selaput lendir hidung, batuk, napas berbunyi, tenggorokan tertutup.
- *Kelainan pada kulit dan lapisan bawah kulit:* Stevens-Johnson syndrome
- *Gangguan umum pada tempat penyuntikan:* rasa gatal, rasa lemah, nyeri pada tungkai, rasa sakit pada dada
- *Gangguan pencernaan:* muntah-muntah

INTERAKSI OBAT
Data evaluasi yang berhubungan dengan pemberian FluQuadri dengan vaksin lain tidak tersedia.

PENGGUNAAN DALAM POPULASI SPESIFIK
Kehamilan
Penelitian reproduksi hewan belum pernah dilakukan dengan FluQuadri. Belum juga diketahui apakah FluQuadri dapat menyebabkan bahaya jika diberikan kepada wanita hamil atau dapat mempengaruhi kemampuan reproduksi.

Ibu menyusui
Belum diketahui apakah FluQuadri dikeluarkan lewat ASI. Karena banyak obat-obatan yang dengan sendirinya dikeluarkan lewat ASI, perhatian khusus diperlukan apabila memberikan FluQuadri kepada Ibu menyusui.

Penggunaan pada Anak-anak
Keamanan dan efektivitas dari FluQuadri pada anak usia 6 bulan ke bawah belum jelas . Profil keamanan dan respon kekebalan dari FluQuadri baru dievaluasi pada anak usia 6 bulan sampai 8 tahun.

Penggunaan pada usia lanjut.
Profil keamanan dan respon kekebalan dari FluQuadri dievaluasi pada manula usia 65 tahun ke atas. [lihat Efek Samping]. Respon antibodi terhadap FluQuadri lebih rendah pada orang usia di atas 65 tahun daripada orang yang lebih muda.

CARA PENGGUNAAN, PENYIMPANAN, KEMASAN DAN PENANGANAN
Cara penggunaan
Alat suntik siap pakai dengan satu dosis (tuas penyuntik berwarna merah muda), tanpa jarum suntik, 0.25 mL, kemasan berisi 5 (tidak dibuat menggunakan bahan latex karet alam).

Alat suntik dengan satu kali dosis (tuas penyuntik berwarna bening), tanpa jarum suntik, 0.5 mL, paket berisi 5 (tidak dibuat menggunakan bahan latex karet alam).

Kemasan
Dus, 5 alat suntik siap pakai @ 0,5 ml (1 dosis) - Adult No. Reg.: DKI1616500243B1
Dus, 5 alat suntik siap pakai@ 0,25 ml (1 dosis) - Pediatric No. Reg.: DKI1616500243A1

Penyimpanan dan penanganan
Simpan FluQuadri dalam kulkas pada suhu 2° sampai 8°C (35° sampai 46°F). **JANGAN DIBEKUKAN**. Buang produk apabila sudah sempat beku.
Jangan digunakan setelah lewat dari tanggal kadaluwarsa yang tertera pada label kemasan.
FluQuadri adalah merek dagang dari Sanofi Pasteur Inc.

HARUS DENGAN RESEP DOKTER

Diimport oleh:
PT Aventis Pharma, Jakarta – Indonesia

Diproduksi oleh:
Sanofi Pasteur Inc., Swiftwater PA 18370 USA

Tanggal Revisi Teks:
as on approval date