Flublok Quadrivalent (Influenza Vaccine), Sterile Solution for Intramuscular Injection

2019-2020 Formula

Initial U.S. Approval: 2013

INDICATIONS AND USAGE

Flublok Quadrivalent is a vaccine indicated for active immunization against disease caused by influenza A subtype viruses and influenza type B viruses contained in the vaccine. Flublok Quadrivalent is approved for use in persons 18 years of age and older. (1)

DOSEAGE AND ADMINISTRATION

For intramuscular (IM) injection only (0.5 mL). (2)

DOSEAGE FORMS AND STRENGTHS

A sterile solution for injection supplied in 0.5 mL single dose prefilled syringes. (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine. (4, 6.2, 11)

WARNINGS AND PRECAUTIONS

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of Flublok Quadrivalent. (5.1)

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok Quadrivalent should be based on careful consideration of potential benefits and risks. (5.2)

ADVERSE REACTIONS

In adults 18 through 49 years of age, the most common (≥10%) injection-site reactions were tenderness (48%) and pain (37%); the most common (≥10%) solicited systemic adverse reactions were headache (20%), fatigue (17%), myalgia (13%) and arthralgia (10%). (6.1)

In adults 50 years of age and older, the most common (≥10%) injection site reactions were tenderness (34%) and pain (19%); the most common (≥10%) solicited systemic adverse reactions were headache (13%) and fatigue (12%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur Inc., at 1-800-822-2463 (1-800-Vaccine) or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy outcomes in women exposed to Flublok Quadrivalent during pregnancy are being monitored. Contact: Sanofi Pasteur Inc. by calling 1-800-822-2463. (6.1)

See 17 for PATIENT COUNSELING INFORMATION

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

Revised: 05/2020

Flublok Quadrivalent is a sterile solution supplied in prefilled, single-dose syringes, 0.5 mL. (2)

Flublok Quadrivalent is a sterile solution for injection supplied in 0.5 mL single dose prefilled syringes. (3)

Flublok Quadrivalent is a sterile solution for injection supplied in 0.5 mL single dose prefilled syringes. (3)

Flublok Quadrivalent is a sterile solution supplied in prefilled, single-dose syringes, 0.5 mL. (2)

Flublok Quadrivalent is a sterile solution supplied in prefilled, single-dose syringes, 0.5 mL. (2)
Flublok Quadrivalent (n=4328) or Comparator (Fluarix Quadrivalent, manufactured by GlaxoSmithKline) in Adults 50 Years of Age and Older, Study 2 (Reactogenicity Populations)\(^1\) (continued)

<table>
<thead>
<tr>
<th>Reactogenicity Term</th>
<th>Any Grade(^1)</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Any Grade(^1)</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle Pain</td>
<td>9</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>9</td>
<td>&lt;1</td>
<td>&lt;1</td>
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<tr>
<td>Joint Pain</td>
<td>8</td>
<td>&lt;1</td>
<td>0</td>
<td>8</td>
<td>&lt;1</td>
<td>&lt;1</td>
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<tr>
<td>Nausea</td>
<td>5</td>
<td>&lt;1</td>
<td>0</td>
<td>5</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Shivering / Chills</td>
<td>5</td>
<td>&lt;1</td>
<td>0</td>
<td>4</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Fever(^{2,3})</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>0</td>
<td>1</td>
<td>&lt;1</td>
<td>0</td>
</tr>
</tbody>
</table>

NOTE: Data based on the most severe response reported by subjects. Results ≥1% reported to nearest whole percent; results >0 but <1% reported as <1%.

*Comparator = U.S.-licensed comparator quadrivalent inactivated influenza vaccine manufactured by GlaxoSmithKline.

†Study 2 is registered as NCT01439509 under the National Clinical Trials registry.

‡Denominators for fever: Flublok Quadrivalent n = 4262, Comparator n = 4282.

§Denominators for injection site reactions: Flublok Quadrivalent n = 4307, Comparator n = 4319.

\(*\)Denominator for injection site reactions: Flublok Quadrivalent n = 4328, Comparator n = 4327.

\(^{†}\)Fever defined as ≥100.4°F (38°C). Grade 1 (≥100.4°F to <101.1°F); Grade 2 (101.2°F to <102°F); Grade 3 (102.1°F to <104°F); Grade 4 ≥104°F.

Among adults 18-49 years of age (Study 1), through 6 months post-vaccination, no deaths were reported. SAEs were reported by 12 subjects; 10 (11%) Flublok recipients and 2 (2.6%) Comparator recipients. No SAEs were considered related to study vaccine.

Among adults 50 years of age and older (Study 2), 20 deaths occurred in the 6 months post-vaccination, including 8 Flublok Quadrivalent and 12 Comparator recipients. No deaths were considered related to study vaccine. SAEs were reported by 80 subjects (37 Flublok recipients and 132 (3%) Comparator recipients. No SAEs were considered related to study vaccine.

In the 28 days following vaccination, one or more unsolicited treatment emergent adverse events occurred in 10.3% of Flublok Quadrivalent and 10.5% of Comparator recipients in Study 1 (adults 18-49 years of age) and in 13.9% of Flublok Quadrivalent and 14.1% of Comparator recipients in Study 2 (adults ≥50 years of age). In both studies, rates of individual events were similar between treatment groups, and most events were mild to moderate in severity.

Flublok (Trivalent Formulation)

The safety experience with Flublok is relevant to Flublok Quadrivalent because both vaccines are manufactured using similar manufacturing processes.

Table 2: Frequency of Solicited Local Injection Site Reactions and Systemic Adverse Reactions within 7 Days of Administration of Flublok Quadrivalent or Comparator in Adults 50 Years of Age and Older, Study 2 (Reactogenicity Populations)\(^1\)

<table>
<thead>
<tr>
<th>Reactogenicity Term</th>
<th>Any Grade(^1)</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Any Grade(^1)</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥1 injection site reaction(^1)</td>
<td>38</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>40</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Local Tenderness</td>
<td>34</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>37</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Local Pain</td>
<td>19</td>
<td>&lt;1</td>
<td>0</td>
<td>22</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Firmness / Swelling</td>
<td>3</td>
<td>&lt;1</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Redness</td>
<td>3</td>
<td>&lt;1</td>
<td>0</td>
<td>2</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Subjects with ≥1 systemic reactogenicity event(^1)</td>
<td>25</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>26</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Headache</td>
<td>13</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>14</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12</td>
<td>&lt;1</td>
<td>0</td>
<td>12</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

NOTE: Data based on the most severe response reported by subjects. Results ≥1% reported to nearest whole percent; results >0 but <1% reported as <1%.

*Comparator = U.S.-licensed comparator quadrivalent inactivated influenza vaccine, Fluvarix Quadrivalent, manufactured by GlaxoSmithKline.

†Study 2 is registered as NCT02236958 under the National Clinical Trials registry.

‡Reactogenicity Populations were defined as all randomized subjects who received study vaccine (according to the treatment actually received and who had at least one non-missing data point for injection site, systemic or body temperature reactogenicity categories. For local pain, tenderness, and systemic reactions: Grade 1 = No interference with activity. Grade 2 = Some interference with activity. Grade 3 = Prevents daily activity; Grade 4 = Required ER visit or hospitalization. For injection site redness and firmness/swelling: Grade 1 = 10 to <50 mm (small). Grade 2 = 51 to <100 mm (medium). Grade 3 = ≥100 mm (large). Grade 4 = necrosis or exfoliative dermatitis.

§Denominators for injection site reactions: Flublok Quadrivalent n = 4307, Comparator n = 4319.

\(*\)Denominators for systemic reactions: Flublok Quadrivalent n = 4306, Comparator n = 4318.

\(^{†}\)Denominators for fever: Flublok Quadrivalent n = 4328, Comparator n = 4327.

\(^{‡}\)Fever defined as ≥100.4°F (38°C). Grade 1 (≥100.4°F to <101.1°F); Grade 2 (101.2°F to <102°F); Grade 3 (102.1°F to <104°F); Grade 4 ≥104°F.

Any Grade/\(^1\) reported as <1% to nearest whole percent; results >0 but <1% reported as <1%.

Flublok (Trivalent Formulation) has been evaluated in six clinical trials (Studies 3-7): 2497 adults 18 through 49 years, 972 adults 50 through 64 years, and 1078 adults 65 years and older. In Studies 3-5 and 7, SAEs were collected for 6 months post-vaccination. Study 6 collected SAEs through 30 days following receipt of vaccine. Study 6 also actively solicited pre-specified common hypersensitivity-type reactions through 30 days following receipt of vaccine as a primary endpoint.

In Studies 3 and 4, 468 subjects 18 through 49 years of age for safety analysis, randomized to receive Flublok (n=2344) or placebo (n=2304) [see Clinical Studies (14)]. Study 4 included 802 subjects 50 through 64 years of age for safety analysis, randomized to receive Flublok (n=303) or another U.S.-licensed trivalent influenza vaccine (Fluzone, manufactured by Sanofi Pasteur, Inc.) as an active control (n=302).

Study 5 included 869 subjects aged 65 years and older for safety analysis, randomized to receive Flublok (n=436) or another U.S.-licensed trivalent influenza vaccine (Fluzone) as an active control (n=433).

Study 6 included 2627 subjects aged 50 years and older for safety analysis, randomized to receive Flublok (n=1314) or another U.S.-licensed trivalent influenza vaccine (Afluria, manufactured by Seqirus Pty Ltd.) as an active control (n=1313). Among subjects 50 through 64 years of age, 672 received Flublok and 665 received Afluria. Among subjects aged 65 years and older, 642 received Flublok and 648 received Afluria.

Study 7 was a Phase 2 dose-finding trial conducted in adults 18 through 49 years of age, 153 of whom received Flublok 135 mcg, the licensed trivalent formulation.

**Serious Adverse Events**

Among 2497 adults 18-49 years of age (Studies 3 and 7 pooled), through 6 months post-vaccination, two deaths were reported, one in a Flublok recipient and one in a placebo recipient. Both deaths occurred within 28 days following vaccination and neither was considered vaccine-related. SAEs were reported by 32 Flublok recipients and 35 placebo recipients. One SAE (pleural/heart disease) in a Flublok recipient was assessed as possibly related to the vaccine. Among 972 adults 50-64 years of age (Studies 4 and 6 pooled), through up to 6 months post-vaccination, no deaths occurred, and SAEs were reported by 10 subjects, 6 Flublok recipients and 4 Comparator recipients. One of the SAEs, vasovagal syncope following injection of Flublok, was considered related to administration of study vaccine.

Among 1078 adults 65 years of age and older (Studies 5 and 6 pooled), through up to 6 months post-vaccination, 4 deaths occurred, 2 in Flublok recipients and 2 in Comparator recipients. None were considered related to the study vaccines. SAEs were reported by 80 subjects (37 Flublok recipients, 43 Comparator recipients). None were considered related to the study vaccines.
Among 1314 adults 50 years of age and older (Study 7) for whom the incidence of rash, urticaria, swelling, non-pitting edema, or other potential hypersensitivity reactions were actively solicited for 30 days following vaccination, a total of 2.4% of Flublok recipients and 1.6% of Comparator recipients reported such events over the 30 day follow-up period. A total of 1.9% and 0.9% of Flublok and Comparator recipients, respectively, reported these events in the 7 days following vaccination. Of these solicited events, rash was most frequently reported (Flublok 1.3%, Comparator 0.8%) over the 30 day follow-up period.

6.2 Postmarketing Experience

The following events have been spontaneously reported during post-approval use of Flublok Quadrivalent. They are described because of the temporal relationship, the biologic plausibility of a causal relationship to Flublok Quadrivalent, and their potential seriousness. 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.

Immunologic system disorders: anaphylaxis, allergic reactions, and other forms of hypersensitivity (including urticaria).

7 DRUG INTERACTIONS

Data evaluating the concomitant administration of Flublok Quadrivalent with other vaccines are not available.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure

Pregnancy outcomes in women who have been exposed to Flublok Quadrivalent during pregnancy are being monitored. Sanofi-Pasteur Inc. is maintaining a prospective pregnancy exposure registry to collect data on pregnancy outcomes and newborn health status following vaccination with Flublok Quadrivalent during pregnancy. Healthcare providers are encouraged to enroll women who receive Flublok Quadrivalent during pregnancy in Sanofi Pasteur Inc.’s vaccination pregnancy registry by calling 1-800-822-2463.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies are 2% to 4% and 15% to 20%, respectively. Available data on Flublok Quadrivalent and Flublok (trivalent formulation) administered to pregnant women are insufficient to inform vaccine-associated risks in pregnant women. There were no developmental studies of Flublok Quadrivalent formulation performed in animals. The developmental effects of Flublok (trivalent formulation) are relevant to Flublok Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions. A developmental study of Flublok (trivalent formulation) has been performed in rats administered 0.5 mL divided of Flublok (trivalent formulation) prior to mating and during gestation. This study revealed no evidence of harm to the fetus due to Flublok (trivalent formulation) [see Data].

Clinical Considerations

Disease-associated Maternal and/or Embryo/Fetal Risk

Pregnant women are at increased risk of complications associated with influenza infection compared to non-pregnant women. Pregnant women with influenza may be at increased risk for adverse pregnancy outcomes, including preterm labor and delivery.

Data

Animal

In a developmental toxicity study, female rats were administered 0.5 mL divided of Flublok (trivalent formulation) by intramuscular injection twice prior to mating (35 days and 14 days prior to mating) and on gestation Day 6. No vaccine-related fetal malformations or variations or other adverse effects on maternal or fetal well-being were observed in the study.

Data

8.2 Lactation

Lactation

It is not known whether Flublok Quadrivalent is excreted in human milk. Data are not available to assess the effects of Flublok (trivalent formulation) or Flublok Quadrivalent on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for Flublok Quadrivalent and any potential adverse effects on the breastfed child from Flublok Quadrivalent or from the underlying maternal condition. For preventive vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Pediatric Use

Data from a randomized, controlled trial demonstrated that children 6 months to less than 3 years of age had diminished hemagglutinin inhibition (HI) responses to Flublok (trivalent formulation) as compared to a U.S.-licensed influenza vaccine approved for use in this population, strongly suggesting that Flublok (trivalent formulation) would not be as effective as licensed vaccine. The development and effectiveness of Flublok Quadrivalent have not been established in children 3 years to less than 18 years of age.

8.5 Geriatric Use

Geriatric Use

Data from an efficacy study (Study 2), which included 1759 subjects ≥65 years and 525 subjects ≥75 years who received Flublok Quadrivalent, are insufficient to determine whether elderly subjects respond differently from younger subjects [see Clinical Trials Experience (6.1) and Clinical Studies (14)].

11 DESCRIPTION

Flublok Quadrivalent (Quadrivalent Influenza Vaccine) is a sterile, clear, colorless solution of recombinant hemagglutinin (HA) proteins from four influenza viruses for intramuscular injection. It contains purified HA proteins produced in a continuous insect cell line [expressSF®]. That is derived from Sf9 cells of the fall armyworm, Spodoptera frugiperda (which is related to moths, caterpillars and butterflies), and grown in serum-free medium composed of chemically-defined lipids, vitamins, amino acids, and mineral salts. Each of the four HAs is expressed in this cell line using a baculovirus vector (Autographa californica nuclear polyhedrosis virus), extracted from the cells with Triton X-100 and further purified by column chromatography. The purified HAs are then blended and filled into single-dose syringes. Flublok Quadrivalent is standardized according to United States Public Health Service (USPHS) requirements. For the 2019-2020 influenza season it is formulated to contain 190 mcg HA per 0.5 mL dose, with 45 mcg HA of each of the following 4 influenza virus strains: A/Brisbane/02/2018 (H1N1), A/Kansas/14/2017 (H3N2), B/Malaysia/12/2016 (a B/Colorado/6/2017-like virus) and B/Phuket/3073/ 2013. A single 0.5 mL dose of Flublok Quadrivalent contains sodium chloride (4.4 mg), monobasic sodium phosphate (1.5 mg), dibasic sodium phosphate (1.3 mg), and polysorbate 20 (25.7 mcg).

Each 0.5 mL dose of Flublok Quadrivalent may also contain residual amounts of baculovirus and Spodoptera frugiperda cell proteins (<19 mcg), baculovirus and cellular DNA (<10 mcg), and Triton X-100 (<100 mcg).

Flublok Quadrivalent contains no egg proteins, antibiotics, or preservatives. The single-dose, prefilled syringes contain no natural rubber latex.
Study 2 evaluated the efficacy of Flublok Quadrivalent in a randomized, observer-blind, active-controlled, multicenter trial conducted during the 2014-2015 influenza season in adults 50 years of age and older. A total of 8693 healthy, medically stable adults (mean age 62.5 years) were randomized in a 1:1 ratio to receive a single dose of Flublok Quadrivalent (n=4474) or a U.S.-licensed quadrivalent inactivated influenza vaccine (Comparator, Fluarix Quadrivalent, manufactured by GlaxoSmithKline) (n=4489). Among randomized subjects, 58% were female, 80% white, 18% black/African American, 2% other races, and 5% of Hispanic/Latino ethnicity. A total of 5186 (60%) subjects were 50-64 years of age and 3486 (40%) were ≥65 years of age. Real-time polymerase chain reaction (RT-PCR)-confirmed influenza was assessed by post-vaccination surveillance for influenza-like illness (ILI) beginning 2 weeks post-vaccination until the end of the influenza season, approximately 6 months post-vaccination. ILI was defined as having at least one symptom (no specified duration) in each of two categories of respiratory and systemic symptoms. Respiratory symptoms included sore throat, cough, sputum production, wheezing and difficulty breathing. Systemic symptoms included fever (>37.5°C), oral chills, fatigue, headache and myalgia. For subjects with an episode of ILI, a nasopharyngeal swab sample was collected for RT-PCR testing and reflex viral culture of RT-PCR-positive samples. The primary efficacy endpoint of Study 2 was RT-PCR-positive, protocol-defined ILI due to any strain of influenza. Attack rates and relative vaccine efficacy (rVE), defined as 1 − (Attack rate Flublok Quadrivalent/Attack Rate Comparator), were calculated for the total efficacy population (n=8604) for the primary efficacy endpoint and for several alternative efficacy endpoints (Table 4). Antigenic and phylogenetic evaluations of the similarity (“matching”) of clonal isolates to vaccine antigens were not performed. CDC epidemiological influenza season was defined as the period from the first week of occurrence of non-H3N2 viruses predominated and that most influenza A/H3N2 viruses were antigenically dissimilar while A/H1N1 and B viruses were antigenically similar to vaccine antigens.

### Table 5: Comparison of Day 28 Post-Vaccination Geographic Mean Titer (GMT) for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population)^1,4,5

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Post-vaccination GMT Flublok Quadrivalent (N=969)</th>
<th>Post-vaccination Comparator (N=323)</th>
<th>GMT Ratio Flublok/Comparator (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>493</td>
<td>397</td>
<td>1.26 (1.09, 1.44)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>748</td>
<td>377</td>
<td>0.98 (0.74, 1.29)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>156</td>
<td>134</td>
<td>0.99 (0.74, 1.30)</td>
</tr>
</tbody>
</table>

**Abbreviations:** GMT, geometric mean titer. 

^Study 1 is registered as NCT0228509.

### Table 6: Comparison of Day 28 Serovaccination Rates for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population)^4,5

<table>
<thead>
<tr>
<th>Antigen</th>
<th>SCR (%, 95% CI) Flublok Quadrivalent (N=969)</th>
<th>SCR (%, 95% CI) Comparator (N=323)</th>
<th>SCR Difference (%) Flublok Comparator (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>66.7 (63.6, 69.8)</td>
<td>63.5 (58.0, 68.7)</td>
<td>-3.2 (-9.2, 2.8)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>57.0 (51.4, 62.4)</td>
<td>-15.2 (-21.3, -9.1)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>59.6 (56.5, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>0.7 (-5.6, 6.9)</td>
</tr>
</tbody>
</table>

**Abbreviations:** CI, confidence interval; GMT, geometric mean titer. 

^Study 1 is registered as NCT0228509.

### Table 3: Vaccine Efficacy against Culture-Confirmed Influenza in Healthy Adults 18-49 Years of Age, Study 3 (Continued)

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Flublok (trivalent) (N=2344)</th>
<th>Saline Placebo (N=2334)</th>
<th>Flublok Vaccine Efficacy</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, n</td>
<td>23</td>
<td>10</td>
<td>36</td>
<td>1.6</td>
</tr>
</tbody>
</table>

^In Study 3 (NCT00539891) vaccine efficacy analyses were conducted on the Total Vaccinated Cohort (all randomized subjects who received study vaccine according to the treatment actually received and who provided data). Vaccine efficacy (VE) = 1 minus the ratio of Flublok/placebo infection rates. Determined under the assumption of Poisson event rates, according to Breslow and Day, 1987. *Meets CDC influenza-like illness (CDIL-ILI) as defined as fever of ≥100°F oral accompanied by cough and/or sore throat, on the same day or on consecutive days. **Primary endpoint of trial. ↑All culture-confirmed cases are considered, regardless of whether they qualified as CDIL-ILI. ∗Secondary endpoint of trial. ◊Exploratory (prespecified) endpoint of trial. The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that could adversely affect efficacy. The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that could adversely affect efficacy. The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that could adversely affect efficacy. The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that could adversely affect efficacy. The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that could adversely affect efficacy. 

### Table 4: Relative Vaccine Efficacy (rVE) of Flublok Quadrivalent versus Comparator in Adults 18-49 Years of Age, Study 3 (Immunogenicity Population)^1,2

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Scr (%, 95% CI) Flublok Quadrivalent (N=969)</th>
<th>Scr (%, 95% CI) Comparator (N=323)</th>
<th>Scr Difference (%) Flublok Comparator (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>66.7 (63.6, 69.8)</td>
<td>63.5 (58.0, 68.7)</td>
<td>-3.2 (-9.2, 2.8)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>57.0 (51.4, 62.4)</td>
<td>-15.2 (-21.3, -9.1)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>59.6 (56.5, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>0.7 (-5.6, 6.9)</td>
</tr>
</tbody>
</table>
16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied
Flublok Quadrivalent is supplied as a single-dose, 0.5 mL syringe in a 5 or 10 syringe carton:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components and NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-Dose Pre-filled Syringe</td>
<td>49281-719-10</td>
<td>Ten 0.5 mL single-dose prefilled syringes [NDC 49281-719-88]</td>
</tr>
</tbody>
</table>

16.2 Storage and Handling
- Store refrigerated between 2°C and 8°C (36°F and 46°F).
- Do not freeze. Discard if product has been frozen.
- Protect syringes from light.
- Do not use after expiration date shown on the label.

17 PATIENT COUNSELING INFORMATION
Inform the vaccine recipient of the potential benefits and risks of vaccination with Flublok Quadrivalent.
Inform the vaccine recipient that:
- Flublok Quadrivalent contains non-infectious proteins that cannot cause influenza.
- Flublok Quadrivalent stimulates the immune system to produce antibodies that help protect against
  the influenza viruses carrying the proteins contained in the vaccine, but does not prevent other
  respiratory infections.

Instruct the vaccine recipient to report any adverse events to their healthcare provider and/or to the
Vaccine Adverse Event Reporting System (VAERS).
Provide the vaccine recipient with the Vaccine Information Statements which are required by the
National Childhood Vaccine Injury Act of 1986 to be given prior to vaccination. These materials are
available free of charge at the Centers for Disease Control (CDC) website (www.cdc.gov/vaccines).
Encourage women who receive Flublok or Flublok Quadrivalent while pregnant to notify Sanofi Pasteur
Inc. by calling 1-800-822-2463.
Instruct the vaccine recipient that annual vaccination to prevent influenza is recommended.

Manufactured by Protein Sciences Corporation (Meriden, CT).

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INFB4-FPLR-SL-MAY20 Rx Only