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)

DOSAGE AND ADMINISTRATION

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

Dosage

Administer Flublok Quadrivalent as a single 0.5 mL dose.

Administration

Invert the prefilled syringe containing Flublok Quadrivalent gently prior to affixing the appropriate size needle for intramuscular administration. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered. The preferred site for injection is the deltoid muscle. Flublok Quadrivalent should not be mixed in the same syringe with any other vaccine.

Dosage 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)

• 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

Revised: 07/2020

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

9 PATIENT COUNSELING INFORMATION

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2 DOSAGE AND ADMINISTRATION

2.1 Dosage

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4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Managing Allergic Reactions

5.2 Guillain-Barré Syndrome

5.3 Altered Immunocompetence

5.4 Limitations of Vaccine Effectiveness

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Postmarketing Experience

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Flublok Quadrivalent is a vaccine indicated for active immunization against disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. Flublok Quadrivalent is approved for use in persons 18 years of age and older. (see Clinical Studies (14)).

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Dosage

Administer Flublok Quadrivalent as a single 0.5 mL dose.

2.2 Administration

Invert the prefilled syringe containing Flublok Quadrivalent gently prior to affixing the appropriate size needle for intramuscular administration. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered. The preferred site for injection is the deltoid muscle. Flublok Quadrivalent should not be mixed in the same syringe with any other vaccine.

3 DOSAGE FORMS AND STRENGTHS

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

4 CONTRAINDICATIONS

Flublok Quadrivalent is contraindicated in individuals with known severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine (see Postmarketing Experience (6.2) and Description (11)).

5 WARNINGS AND PRECAUTIONS

5.1 Managing Allergic Reactions

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

5.2 Guillain-Barré Syndrome

The 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barré Syndrome (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 one additional case per 1 million persons vaccinated. If GBS has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of the potential benefits and risks.

5.3 Altered Immunocompetence

If Flublok Quadrivalent is administered to immunocompromised individuals, including persons receiving immunosuppressive therapy, the immune response may be diminished.

5.4 Limitations of Vaccine Effectiveness

Vaccination with Flublok Quadrivalent may not protect all vaccine recipients.

6 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%) (see Clinical Trials Experience (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 fatique (12%) (see Clinical Trials Experience (6.1)).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

16.2 Storage and Handling

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed
Study 2 included 8672 subjects 50 years of age and older for safety analysis, randomized to receive Flublok Quadrivalent or the comparator vaccine. Fever defined as ßFever defined as ≥101.3°F; Grade 2=101.3°F to <102.0°F; Grade 3=102.0°F to <104.0°F; Grade 4=104.0°F.

<table>
<thead>
<tr>
<th>Reagocinuity Term</th>
<th>Flublok Quadrivalent</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥1 injection site reaction‡, ¶</td>
<td>Any Grade</td>
<td>Grade 3</td>
</tr>
<tr>
<td></td>
<td>N=996</td>
<td></td>
</tr>
<tr>
<td>Subjects with ≥1 injection site reaction‡, ¶</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Local Tenderness</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Firmness / Swelling</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Fever*</td>
<td>2</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 manufactured by GlaxoSmithKline.
†Study 1 is registered as NCT02290509 under the National Clinical Trials registry.
‡Reagocinuity 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 reagocinuity categories. For local pain, tenderness and systemic reactions: Grade 1 = No interference with activities. Grade 2 = Prevented some activities, and headache may have required non-narcotic pain reliever. Grade 3=Prevented daily activity. Grade 4=Required ER visit or hospitalization. For injection site redness and firmness/swelling: Grade 1=≤50 mm (small). Grade 2=51 to ≤100 mm (medium). Grade 3=101 mm (large). Grade 4=necrosis or exfoliative dermatitis.
¶Denominators for injection site reactions: Flublok Quadrivalent n = 4306, Comparator n = 4318.
#Denominators for systemic reactions: Flublok Quadrivalent n = 4306, Comparator n = 4318.

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 (Reagocinuity Populations) (continued)
Among 972 adults 50-64 years of age (Study 3) 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.

Immune 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 3. No maternal or fetal malformations or variations and no adverse effects on pre-weaning development were observed in the study.

8.2 Lactation

Risk Summary
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

Data from a randomized, controlled trial demonstrated that children 6 months to less than 3 years of age (Study 4) and children 4 years of age and older (Study 5) had Flublok (trivalent formulation) 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 effective in children younger than 3 years of age. Safety and effectiveness of Flublok Quadrivalent have not been established in children 3 years to less than 18 years of age.

8.5 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 recombining hemagglutinin (HA) proteins from four influenza viruses for intramuscular injection. It contains purified HA proteins produced in a continuous insect cell line (expressed [7]) 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 2020-2021 influenza season it is formulated to contain 180 mcg HA per 0.5 mL dose, with 45 mcg HA of each of the following 4 influenza virus strains: A/Hawaii/70/2019 (H1N1), A/Hinshaw/1/2019 (A/Hong Kong/45/1997-like virus) (H3N2), B/Washington/02/2019 and B/Phuket/3073/2013.

A single 0.5 mL dose of Flublok Quadrivalent contains sodium chloride (4.4 mg), monobasic sodium phosphate (0.195 mg), dibasic sodium phosphate (1.3 mg), and polysorbate 20 (Tweeñ® 27.5 mcg). Each 0.5 mL dose of Flublok Quadrivalent may also contain residual amounts of baculovirus and Spodoptera frugiperda cell proteins (≤13 mcg), baculovirus and cellular DNA ≤(10 mcg)5, and Triton X-100 ≤(100 mcg).

Flublok Quadrivalent contains no egg proteins, antibiotics, or preservatives. The single-dose, prefilled syringe contains no natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Flublok Quadrivalent contains recombinant HA proteins of the four strains of influenza virus specified by health authorities for inclusion in the annual seasonal vaccine. These proteins function as antigens which induce a humoral immune response, measured by hemagglutination inhibition (HI) antibody. 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 (usually annual) development of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the usual replacement of one or more influenza virus strains in each year’s influenza vaccine. Therefore, influenza vaccines are standardized to contain the hemagglutinins of influenza virus strains (i.e., typically two type A and, in quadrivalent formulations, two type B), representing the influenza viruses likely to be circulating in the U.S. in the upcoming winter.

13 NONCLINICAL STUDIES

Flublok Quadrivalent has not been evaluated for carcinogenic or mutagenic potential, or for impairment of male fertility in animals. A developmental toxicity study conducted in rats vaccinated with Flublok (trivalent formulation) revealed no evidence of impaired female fertility [see Pregnancy (8.1)]

14 CLINICAL STUDIES

14.1 Efficacy against Laboratory-Confirmed Influenza

The efficacy of Flublok (trivalent formulation) is relevant to Flublok Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions [see Description (11)]. The efficacy of Flublok (trivalent formulation) in protecting against influenza illness was evaluated in a randomized, observer-blind, placebo-controlled multicenter trial conducted in the U.S. during the 2006-2007 influenza season in adults 18-49 years of age (Study 3). Study 3 enrolled and vaccinated 4648 healthy adults (mean age 29.5 years) randomized in a 1:1 ratio to receive a single dose of Flublok (n=2344) or saline placebo (n=2304). Among enrolled subjects, 59% were female, 67% were white, 19% African-American, 2% Asian, <1% other races, and 11% of Latino/Hispanic ethnicity. Culture-confirmed influenza was assessed by active and passive surveillance for influenza-like illness (ILI) beginning 2 weeks post-vaccination until the end of the influenza season, approximately 7 months post-vaccination.ILI was defined as having at least 2 of 3 symptoms (no specified duration) in the following categories: 1) fever ≥100°F; 2) respiratory symptoms (cough, sore throat or runny nose/stuffy nose); or 3) systemic symptoms (myalgias, arthralgias, headache, chills/fever, or tiredness/malaise). For subjects with an episode of ILI, nasal and throat swab samples were collected for viral culture.

The primary efficacy endpoint of Study 3 was Centers for Disease Control-defined influenza-like illness (CDC-ILI) with a positive culture for an influenza virus strain antigenically resembling a strain represented in Flublok. CDC-ILI is defined as fever of ≥100°F oral accompanied by cough, sore throat, or both on the same day or on consecutive days. Attack rates and vaccine efficacy (VE), defined as the reduction in the influenza rate for Flublok relative to placebo, were calculated for the total vaccinated cohort (n=4648).

The pre-defined success criterion for the primary efficacy analysis was that the lower bound of the 95% confidence interval (CI) of VE should be at least 40%. Vaccine efficacy against antigenically matched culture-confirmed CDC-ILI could not be determined relatively because 96% of the influenza isolates obtained from subjects in Study 3 were not antigenically matched to the strains represented in the vaccine. An exploratory analysis of VE of Flublok against all strains, regardless of antigenic match, isolated from any subject with an ILI, not necessarily meeting CDC-ILI criteria, demonstrated an efficacy estimate of 44.8% (95% CI 24.4, 60.0). See Table 3 for a presentation of VE by case definition and antigenic similarity.

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

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Flublok (trivalent) (N=2344)</th>
<th>Saline Placebo (N=2304)</th>
<th>Flublok Vaccine1, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive culture with a strain represented in the vaccine</td>
<td>64 2.7</td>
<td>114 4.9</td>
<td>44.8 (24.4, 60.0)</td>
</tr>
<tr>
<td>CDC-ILI, all matched strains6,5</td>
<td>44 1.9</td>
<td>78 3.4</td>
<td>44.6 (18.8, 62.6)</td>
</tr>
<tr>
<td>Sub-Type A</td>
<td>26 1.1</td>
<td>56 2.4</td>
<td>54.4 (26.1, 72.5)</td>
</tr>
<tr>
<td>Type B</td>
<td>18 0.8</td>
<td>23 1.0</td>
<td>23.1 (-40.0, 69.9)</td>
</tr>
<tr>
<td>Any ILI, all matched strains6,5</td>
<td>64 2.7</td>
<td>114 4.9</td>
<td>44.8 (24.4, 60.0)</td>
</tr>
</tbody>
</table>
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=2304)</th>
<th>Flublok Vaccine Efficacy†</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Type A</td>
<td>41</td>
<td>1.7</td>
<td>79</td>
<td>3.4</td>
</tr>
<tr>
<td>Type B</td>
<td>23</td>
<td>1.0</td>
<td>36</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*In Study 3 (NCT00539981) 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. †Determines under the assumption of Poisson event rates, according to Breslow and Day, 1987. ‡Meets CDC influenza-like illness (CDC-ILI) defined as fever of ≥100°F oral accompanied by cough and/or sore throat, on the same day or on consecutive days.

Table 4: Relative Vaccine Efficacy (rVE) of Flublok Quadrivalent versus Comparator against Laboratory-Confirmed Influenza, Regardless of Antigenic Similarity to Vaccine Antigens, Adults 50 Years of Age and Older, Study 2 (Efficacy Population) †, ‡, §

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Comparator</th>
<th>Flublok Quadrivalent</th>
<th>rVE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>156</td>
<td>43</td>
<td>(1.12, 1.71)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>748</td>
<td>74</td>
<td>(0.04, 0.57)</td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>134</td>
<td>64</td>
<td>(0.70, 0.99)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>43</td>
<td>43</td>
<td>(1.29, 1.71)</td>
</tr>
</tbody>
</table>

Table 5: Comparison of Day 28 Post-Vaccination Geometric Mean Titer (GMT) for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population) †, ‡, §

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Post-vaccination</th>
<th>GMT Flublok Quadrivalent (N=962)</th>
<th>Post-vaccination</th>
<th>GMT Comparator (N=323)</th>
<th>GMT Ratio Comparator/Flublok Quadrivalent (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>493</td>
<td>397</td>
<td>0.81</td>
<td>(0.71, 0.92)</td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>748</td>
<td>377</td>
<td>0.50</td>
<td>(0.46, 0.57)</td>
<td></td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>156</td>
<td>134</td>
<td>0.92</td>
<td>(0.76, 1.10)</td>
<td></td>
</tr>
<tr>
<td>B/Victoria</td>
<td>43</td>
<td>64</td>
<td>1.49</td>
<td>(1.29, 1.71)</td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Comparison of Day 28 Seroconversion Rates for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population) †, ‡, §

<table>
<thead>
<tr>
<th>Antigen</th>
<th>SCR (%), 95% CI</th>
<th>Flublok Quadrivalent (N=969)</th>
<th>SCR (%), 95% CI</th>
<th>Comparator (N=323)</th>
<th>SCR Difference (%) Comparator/Flublok Quadrivalent (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</td>
<td>(-3.2, 2.8)</td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>50.7 (51.4, 62.4)</td>
<td>-15.2</td>
<td>(-21.3, -9.1)</td>
<td></td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>59.6 (56.5, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>-0.7</td>
<td>(-5.4, 6.9)</td>
<td></td>
</tr>
<tr>
<td>B/Victoria</td>
<td>40.6 (37.4, 43.7)</td>
<td>58.2 (52.6, 63.6)</td>
<td>17.6</td>
<td>(11.4, 23.9)</td>
<td></td>
</tr>
</tbody>
</table>

GlaxoSmithKline in a randomized, observer-blind, active-controlled, multicenter trial conducted during the 2014-2015 influenza season in healthy adults 18-49 years of age. A total of 1350 subjects were enrolled, randomized 3:1, and vaccinated with Flublok Quadrivalent (998 subjects) or Comparator (332 subjects). Subjects were predominantly female (95%), white (80%), black/African American (37%), and of non-Hispanic/Latino ethnicity (84%), with a mean age of 35.5 years. Of the total vaccinated population, 992 subjects (98% of Flublok and 323 IVIVC recipients, respectively) were evaluable for immune responses (Immunogenicity Population).

Post-vaccination immunogenicity was evaluated on sera obtained 28 days after administration of a single dose of study vaccine. Hemagglutination inhibition (HI) geometric mean titer (GMTs) were determined for the two vaccine groups for each vaccine antigen. Immunogenicity was compared by calculating the difference in seroconversion rates (SCR) and the ratios of GMTs of Comparator to Flublok Quadrivalent. Seroconversion was defined as either a pre-vaccination HI titer of <1:10 and a post-vaccination HI titer of ≥1:20 or a pre-vaccination HI titer of ≥1:20 and a minimum 4-fold rise in post-vaccination HI titer, at Day 28.

Table 7: Post-Vaccination Seroconversion Rates for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population) †, ‡, §

<table>
<thead>
<tr>
<th>Antigen</th>
<th>SCR (%), 95% CI</th>
<th>Flublok Quadrivalent (N=969)</th>
<th>SCR (%), 95% CI</th>
<th>Comparator (N=323)</th>
<th>SCR Difference (%) Comparator/Flublok Quadrivalent (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>64.7 (62.1, 67.4)</td>
<td>63.5 (58.0, 68.7)</td>
<td>1.2</td>
<td>(0.3, 2.1)</td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>50.7 (51.4, 62.4)</td>
<td>-15.2</td>
<td>(-21.3, -9.1)</td>
<td></td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>59.6 (56.5, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>-0.7</td>
<td>(-5.4, 6.9)</td>
<td></td>
</tr>
<tr>
<td>B/Victoria</td>
<td>40.6 (37.4, 43.7)</td>
<td>58.2 (52.6, 63.6)</td>
<td>17.6</td>
<td>(11.4, 23.9)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; GMT, geometric mean titer. †Study 1 is registered as NCT02280509. †The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 5 and Day 28 within specified windows, and had no major protocol deviations that might adversely affect the immune response. The pre-defined success criterion for the GMT ratio of Comparator to Flublok Quadrivalent was that the upper bound of the 2-sided 95% CI of the GMT ratio, GMT Comparator/GMT Flublok Quadrivalent at 28 days post-vaccination, must not exceed 1.5. †HI titer were assayed using egg-derived antigens. §Comparator: U.S.-licensed quadrivalent inactivated influenza vaccine, Fluarix Quadrivalent, manufactured by GlaxoSmithKline.

Success in meeting the seroconversion rate (SCR) endpoint was pre-defined as an upper bound (UB) of the two-sided 95% CI of SCR Comparator – SCR Flublok Quadrivalent ≤10%. Flublok Quadrivalent met the success criterion for SCRs for three of the four antigens but not for the B/Victoria lineage antigen (Table 6). Sub-population analyses of immunogenicity did not reveal significant differences between genders. Sub-analyses according to race and ethnicity were not informative because the sizes of the subsets were insufficient to reach meaningful conclusions. The HI response to the B/Victoria lineage antigen was low in both vaccine groups.
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 Premixed Syringe</td>
<td>49281-720-10</td>
<td>Ten 0.5 mL single-dose prefilled syringes [NDC 49281-720-88]</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.

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