FLUCELVAX QUADRIVALENT (Influenza Vaccine)
Suspension for Intramuscular Injection
2020-2021 Formula
Initial U.S. Approval: 23 May 2016

Indications and Usage (1) 03/2021
Dosage and Administration (2.1) 03/2021

INDICATIONS AND USAGE
FLUCELVAX QUADRIVALENT is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. (1)

For intramuscular use only

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 through 8 years of age</td>
<td>One or two doses*; 0.5 mL each</td>
<td>If 2 doses, administer at least 4 weeks apart</td>
</tr>
<tr>
<td>9 years of age and older</td>
<td>One dose, 0.5 mL</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

*1 or 2 doses depend on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.

Dosage Forms and Strengths
- 0.5 mL single-dose pre-filled syringes. (3, 11)
- 5 mL multi-dose vial containing 10 doses (each dose is 0.5 mL). (3, 11)

Contraindications
History of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine. (4, 11)

Warnings and Precautions
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUCELVAX QUADRIVALENT should be based on careful consideration of the potential benefits and risks. (5.1)

Adverse Reactions
- In adults 18 through 64 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (≥ 40%), erythema and induration (≥ 10%). The most common systemic adverse events were headache, fatigue, and myalgia (≥ 10%). (6)
- In adults ≥ 65 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (≥ 20%) and erythema (≥ 10%). (6)
- In children 2 through 8 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (28.7%), pain (27.9%), and erythema (21.3%), induration (14.9%) and ecchymosis (10.0%). The most common systemic adverse events were sleepiness (14.9%), headache (13.8%), fatigue (13.8%), irritability (13.8%) and loss of appetite (10.6%). (6)
- In children and adolescents 9 through 17 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were injection site pain (21.7%), erythema (17.2%) and induration (10.5%). The most common systemic adverse events were headache (18.1%) and fatigue (17.0%). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Seqirus at 1-855-358-8966 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

Use in Specific Populations
- Geriatric Use: Antibody responses were lower in adults 65 years and older than in younger adults. (8.5)

See 17 for PATIENT COUNSELING INFORMATION. Revised: 03/2021

Full Prescribing Information: Contents*
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FLUCELVAX QUADRIVALENT is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUCELVAX QUADRIVALENT is approved for use in persons 2 years of age and older. [see Clinical Studies (14)]

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

2.1 Dosage and Schedule

Administer FLUCELVAX QUADRIVALENT as a single 0.5 mL intramuscular injection.

Table 1: Dosage and Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 through 8 years of age</td>
<td>One or two doses¹, 0.5 mL each</td>
<td>If 2 doses, administer at least 4 weeks apart</td>
</tr>
<tr>
<td>9 years of age and older</td>
<td>One dose, 0.5mL</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

¹ or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.

2.2 Administration

Shake the syringe vigorously before administering and shake the multi-dose vial preparation each time before withdrawing a dose of vaccine. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. [see Description (11)] If either condition exists, do not administer the vaccine. Between uses, return the multi-dose vial to the recommended storage conditions between 2° and 8°C (36°F and 46°F). Do not freeze. Discard if the vaccine has been frozen.

Attach a sterile needle to the pre-filled syringe. For the multi-dose vial, a separate sterile syringe and needle must be used for each injection to prevent transmission of infectious agents from one person to another. Needles should be disposed of properly and not recapped. It is recommended that small syringes (0.5 mL or 1 mL) should be used to minimize any product loss.

Administer intramuscularly only, preferably in the region of the deltoid muscle of the upper arm. Younger children with insufficient deltoid mass should be vaccinated in the anterolateral aspect of the thigh. Do not inject the vaccine in the gluteal region or areas where there may be a major nerve trunk. Do not administer this product intravenously, intraderally or subcutaneously.

3 DOSAGE FORMS AND STRENGTHS

FLUCELVAX QUADRIVALENT is a suspension for injection supplied in two presentations:

- a 0.5 mL single-dose pre-filled Luer Lock syringe
- a 5 mL multi-dose vial containing 10 doses (each dose is 0.5 mL)

4 CONTRAINDICATIONS

Do not administer FLUCELVAX QUADRIVALENT to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine [see Description (11)].

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

The 1976 swine influenza vaccine was associated with an elevated risk 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 1 additional case per million persons vaccinated. If GBS has occurred after receipt of a prior influenza vaccine, the decision to give FLUCELVAX QUADRIVALENT should be based on careful consideration of the potential benefits and risks.

5.2 Preventing and Managing Allergic Reactions

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

5.3 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines, including FLUCELVAX QUADRIVALENT. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope by maintaining a supine or Trendelenburg position.

5.4 Advanced Immunocompromise

After vaccination with FLUCELVAX QUADRIVALENT, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response.

5.5 Limitations of Vaccine Effectiveness

Vaccination with FLUCELVAX QUADRIVALENT may not protect all vaccine recipients against influenza disease.

6 ADVERSE REACTIONS

In adults 18 through 64 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported (≥ 10%) injection-site adverse reactions were pain (≥ 40%), erythema and induration (≥ 10%). The most common systemic adverse events were headache, fatigue and myalgia (≥ 10%).

In adults ≥ 65 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (≥ 20%) and erythema (≥ 10%).

In children 2 through 8 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (28.7%), pain (27.9%) and erythema (21.3%), induration (14.9%) and ecchymosis (10.0%). The most common systemic adverse events were sleepiness (14.9%), headache (13.8%), fatigue (13.8%), irritability (13.8%) and loss of appetite (10.6%).

In children and adolescents 9 through 17 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were injection site pain (21.7%), erythema (17.2%) and induration (10.5%). The most common systemic adverse events were headache (18.1%) and fatigue (17.0%).

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to rates in clinical studies of another vaccine and may not reflect rates observed in clinical practice.

Adults 18 years of age and older:

The safety of FLUCELVAX QUADRIVALENT in adults was evaluated in a randomized, double-blind, controlled trial conducted in the US (Study 1). The safety population included a total of 2680 adults 18 years of age and older; 1340 adults 18 through 64 years of age and 1340 adults 65 years of age and older.

In this study, adults received FLUCELVAX QUADRIVALENT or one of the two formulations of comparator trivalent influenza vaccine (TIV1c and TIV2c) (FLUCELVAX QUADRIVALENT (N=1335), TIV1c, N=676 or TIV2c, N=669). The mean age of adults who received FLUCELVAX QUADRIVALENT was 57.4 years of age; 54.8% of adults were female and 75.6% were Caucasian, 13.4% were Black, 9.1% were Hispanics, 0.7% were American Indian and 0.3%, 0.1% and 0.7% were Asian, Native Hawaiian and others, respectively. The safety data observed are summarized in Table 2.

In this study, solicited injection site and systemic adverse reactions were collected from adults who completed a symptom diary card for 7 days following vaccination. Solicited adverse reactions for FLUCELVAX QUADRIVALENT and comparator are summarized in Table 2.

Table 2: Incidence of Solicited Adverse Reactions in the Adult Safety Population¹ Reported Within 7 Days of Vaccination (Study 1)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>FLUCELVAX QUADRIVALENT</th>
<th>TIV1c N=330</th>
<th>TIV2c N=327</th>
<th>FLUCELVAX QUADRIVALENT</th>
<th>TIV1c N=340</th>
<th>TIV2c N=336</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>45.4%</td>
<td>43.0%</td>
<td>45.7%</td>
<td>44.5%</td>
<td>43.0%</td>
<td>42.8%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15.4%</td>
<td>15.4%</td>
<td>15.5%</td>
<td>15.2%</td>
<td>15.4%</td>
<td>15.3%</td>
</tr>
<tr>
<td>Headache</td>
<td>18.7%</td>
<td>18.7%</td>
<td>18.7%</td>
<td>18.7%</td>
<td>18.7%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Nausea</td>
<td>9.7%</td>
<td>9.9%</td>
<td>9.5%</td>
<td>9.7%</td>
<td>9.6%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.6%</td>
<td>2.7%</td>
<td>2.7%</td>
<td>2.8%</td>
<td>2.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>5.6%</td>
<td>5.7%</td>
<td>5.7%</td>
<td>5.5%</td>
<td>5.6%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15.4%</td>
<td>15.4%</td>
<td>15.5%</td>
<td>15.5%</td>
<td>15.5%</td>
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<td>2.8%</td>
<td>2.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Fatigue</td>
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<td>15.4%</td>
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<td>2.7%</td>
<td>2.8%</td>
<td>2.7%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

Systemic Adverse Reactions²

- Headache
- Fatigue
- Myalgia
- Nausea
- Vomiting

Abbreviations: Gr 3, Grade 3.

N = number of participants in the Safety Population for each study vaccine group

¹ Safety population: all participants in the exposed population who provided post-vaccination safety data

² Proportion of participants reporting each solicited local adverse reaction or systemic adverse event by study vaccine group based on the number of participants contributing any follow up safety information for at least one data value of an individual sign/symptom

Local Adverse Reactions²

- Pain
- Other
- Fatigue
- Myalgia
- Nausea
- Vomiting
- Fever

Systemic Adverse Reactions²

- Headache
- Fatigue
- Myalgia
- Nausea
- Vomiting
- Fever

Abbreviations: Gr 3, Grade 3.

N = number of participants in the Safety Population for each study vaccine group
Unsolicited adverse events were collected for 21 days after vaccination. In adults 18 years of age and older, unsolicited adverse events were reported in 16.1% of adults who received FLUCELVAX QUADRIVALENT, within 21 days after vaccination.

In adults 18 years of age and older, serious adverse events (SAEs) were collected throughout the study duration (until 6 months after vaccination) and were reported by 3.9%, of the adults who received FLUCELVAX QUADRIVALENT. None of the SAEs were assessed as being related to study vaccine.

Children and Adolescents 2 through 17 years of age:

The safety of FLUCELVAX QUADRIVALENT was evaluated in children and adolescents in Study 2. Study 2 was a multi-season, multi-national (Australia, Estonia, Finland, Lithuania, Philippines, Poland, Spain, Thailand), randomized, observer-blind study in children and adolescents 2 through 17 years of age. The solicited safety population included a total of 4509 children and adolescents 2 through 17 years of age who received FLUCELVAX QW (N=2255) or a non-influenza (meningococcal Groups A, C, Y, and W-135) oligosaccharide diphtheria CRM197 conjugate comparator vaccine (N=2254).

Children 2 through 8 years of age received one or two doses (separated by 4 weeks) of FLUCELVAX QUADRIVALENT or comparator vaccine depending on the subject’s prior influenza vaccination history. Children in the 2-dose comparator group received non-influenza comparator as the first dose and saline placebo as the second dose. Children and adolescents 9 through 17 years of age received a single dose of FLUCELVAX QUADRIVALENT or non-influenza comparator vaccine.

In this study, solicited local injection site and systemic adverse reactions were collected from children and adolescents who completed a symptom diary card for 7 days following vaccination. In children 2 through 8 and children and adolescents 9 through 17 years of age, the incidence of local and systemic solicited adverse reactions reported by children and adolescents who received FLUCELVAX QUADRIVALENT and comparator are summarized in Table 3.

Unsolicited adverse events were collected for 21 days after vaccination. In adults 18 years of age and older, unsolicited adverse events were reported in 16.1% of adults who received FLUCELVAX QUADRIVALENT, within 21 days after vaccination.

In adults 18 years of age and older, serious adverse events (SAEs) were collected throughout the study duration (until 6 months after last vaccination) and were reported by 1.1% of the children and adolescents who received FLUCELVAX QUADRIVALENT. None of the SAEs were assessed as being related to study vaccine.

6.2 Postmarketing Experience

The following additional adverse events have been identified during post-approval use of FLUCELVAX QUADRIVALENT. 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 the vaccine.

- **Immune system disorders:** Allergic or immediate hypersensitivity reactions, including anaphylactic shock.
- **Nervous system disorders:** Syncope, presyncope, paresthesia.
- **Skin and subcutaneous tissue disorders:** Generalized skin reactions including pruritus, urticaria or non-specific rash.

**General disorders and administration site conditions:** Extensive swelling of injected limb.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

**Risk Summary**

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. There are insufficient data for FLUCELVAX QUADRIVALENT in pregnant women to inform vaccine-associated risks in pregnancy.

There were no developmental toxicity studies of FLUCELVAX QUADRIVALENT performed in animals. A developmental toxicity study has been performed in female rabbits administered FLUCELVAX (trivalent formulation) prior to mating and during gestation. The dose was 0.5 mL on each occasion (a single human dose is 0.5 mL). This study revealed no evidence of harm to the fetus due to FLUCELVAX (trivalent formulation).

**Clinical Considerations**

- **Disease-associated Maternal and/or Embryo-Fetal Risk**
  - Pregnant women are at increased risk for severe illness due to influenza 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 Data**
  - In a developmental toxicity study, female rabbits were administered FLUCELVAX (trivalent formulation) by intramuscular injection 1, 3, and 5 weeks prior to mating, and on gestation days 7 and 20. The dose was 0.5 mL on each occasion (a single human dose is 0.5 mL). No vaccine-related 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 FLUCELVAX QUADRIVALENT is excreted in human milk. Data are not available to assess the effects of FLUCELVAX 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 FLUCELVAX QUADRIVALENT and any potential adverse effects on the breastfed child from FLUCELVAX QUADRIVALENT or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine or the effects on milk production.

8.4 Pediatric Use

Safety and effectiveness have not been established in children less than 2 years of age.

8.5 Geriatric Use

Of the total number of adults who received one dose of FLUCELVAX QUADRIVALENT in clinical studies and included in the safety population (2493), 26% (660) were 65 years of age and older and 8% (194) were 75 years of age or older. Antibody responses to FLUCELVAX QUADRIVALENT were lower in the geriatric (adults 65 years and older) population than in younger adults. [see Clinical Studies (14.3)]

11 DESCRIPTION

FLUCELVAX QUADRIVALENT (Influenza Vaccine) is a subunit influenza vaccine manufactured using cell derived candidate vaccine viruses (CV) that are propagated in Madin Darby Canine Kidney (MDCK) cells, a continuous cell line. These cells were adapted to grow freely in suspension in culture medium. The virus is inactivated with the detergent cetyltrimethylammonium bromide and purified through several process steps.

Each of the 4 virus strains is produced and purified separately then pooled to formulate the quadrivalent vaccine.

FLUCELVAX QUADRIVALENT is a sterile, slightly opalescent suspension in phosphate buffered saline. FLUCELVAX QUADRIVALENT is standardized according to United States
The efficacy experience with FLUCELVAX is relevant to FLUCELVAX QUADRIVALENT because both vaccines are manufactured using the same process and have overlapping compositions. A multinational (US, Finland, and Poland), randomized, observer-blind, placebo-controlled trial was performed to assess clinical efficacy and safety of FLUCELVAX during the 2007-2008 influenza season in adults aged 18 through 49 years (Study 3). A total of 11,404 adults were enrolled to receive FLUCELVAX (N=3828), AGRIFLU (N=3676) or placebo (N=3900) in a 1:1:1 ratio. Among the overall study population enrolled, the mean age was 33 years, 55% were female, 84% were Caucasian, 7% were Black, 7% were Hispanic, and 2% were of other ethnic origin.

FLUCELVAX efficacy was assessed by the prevention of culture-confirmed symptomatic influenza illness caused by viruses antigenically matched to those in the vaccine and protection from influenza illness caused by viruses antigenically unmatched to those in the vaccine. Influenza cases were identified by active and passive surveillance of influenza-like illness and confirmed by cell culture and/or real-time polymerase chain reaction (RT-PCR). ILI was defined as a fever (oral temperature ≥ 100.0°F / 38°C) and cough or sore throat. Nasal and throat swab samples were collected for analysis within 120 hours of onset of illness. ILI cases were identified by active and passive surveillance of influenza-like illness (ILI) and confirmed by cell culture and/or real-time polymerase chain reaction (RT-PCR). ILI was defined as a fever (oral temperature ≥ 100.0°F / 38°C) and cough or sore throat. Nasal and throat swab samples were collected for analysis within 120 hours of onset of influenza-like illness in the period from 21 days to 6 months after vaccination.

Overall vaccine efficacy against all influenza viral subtypes and vaccine efficacy against individual influenza viral subtypes were calculated (Tables 4 and 5, respectively).

### Table 4: Vaccine Efficacy against Culture-Confirmed Influenza in Participants aged 18 through 49 years (Study 3)

<table>
<thead>
<tr>
<th>Subtype</th>
<th>FLUCELVAX</th>
<th>Placebo</th>
<th>Vaccine Efficacy (VE)¹²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of participants per protocol</td>
<td>Number of participants with influenza</td>
<td>Attack Rate (%)</td>
</tr>
<tr>
<td>Antigenically Matched</td>
<td>N=3776</td>
<td>7</td>
<td>0.19</td>
</tr>
<tr>
<td>Strains</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H1N1</td>
<td>3843</td>
<td>44</td>
<td>1.14</td>
</tr>
<tr>
<td>B³</td>
<td>3843</td>
<td>140</td>
<td>3.64</td>
</tr>
<tr>
<td>All Culture-Confirmed</td>
<td>N=3776</td>
<td>42</td>
<td>1.11</td>
</tr>
<tr>
<td>Influenza</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H1N1</td>
<td>3843</td>
<td>140</td>
<td>3.64</td>
</tr>
</tbody>
</table>

¹Efficacy against influenza was evaluated over a 9-month period in 2007/2008
²Simultaneous one-sided 97.5% confidence intervals for the vaccine efficacy (VE) of FLUCELVAX relative to placebo based on the Sidak-corrected score confidence intervals for the relative risk. Vaccine Efficacy = (1 – Relative Risk) x 100 %
³VE success criterion: the lower limit of the one-sided 97.5% CI for the estimate of the VE relative to placebo is >40%

### Table 5: Efficacy of FLUCELVAX against Culture-Confirmed Influenza by Influenza Viral Subtype in Participants aged 18 through 49 years (Study 3)

<table>
<thead>
<tr>
<th>Subtype</th>
<th>FLUCELVAX (N=3776)</th>
<th>Placebo (N=3843)</th>
<th>Vaccine Efficacy (VE)²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Attack Rate (%)</td>
<td>Number of Participants with Influenza</td>
<td>Attack Rate (%)</td>
</tr>
<tr>
<td>Antigenically Matched</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H1N1</td>
<td>0.05</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>B³</td>
<td>0.13</td>
<td>5</td>
<td>1.12</td>
</tr>
<tr>
<td>All Culture-Confirmed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H1N1</td>
<td>0.16</td>
<td>6</td>
<td>0.65</td>
</tr>
<tr>
<td>A/H1N2</td>
<td>0.16</td>
<td>6</td>
<td>1.48</td>
</tr>
<tr>
<td>B</td>
<td>0.79</td>
<td>30</td>
<td>1.59</td>
</tr>
</tbody>
</table>

¹No VE success criterion was prespecified in the protocol for each individual influenza virus subtype.
²Simultaneous one-sided 97.5% confidence intervals for the vaccine efficacy (VE) of FLUCELVAX relative to placebo based on the Sidak-corrected score confidence intervals for the relative risk. Vaccine Efficacy = (1 – Relative Risk) x 100 %
³There were too few cases of influenza due to vaccine-matched influenza A/H1N2 or B to adequately assess vaccine efficacy Study 3: NCT00630331
Table 6: Efficacy of FLUCELVAX QUADRIVALENT Against First Occurrence RT-PCR Confirmed or Culture Confirmed Influenza in Participants 2 through 17 years of age—FAS Efficacy (Study 2).2

<table>
<thead>
<tr>
<th>Vaccine Group</th>
<th>Number of cases of influenza</th>
<th>Attack Rate (%)</th>
<th>Vaccine Efficacy (VE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=677 or TIV2c, N=669)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
|               | In the per protocol set, the mean age of adults who received FLUCELVAX QUADRIVALENT (N=1334), TIV1c, TIV2c, N=677 or TIV2c, N=669). In the per protocol set, the mean age of adults who received FLUCELVAX QUADRIVALENT was 9.8 years; 47% of children and adolescents were female and 54% of children and adolescents were Caucasian; 22% were black and 19% were Hispanics. The immune response to each of the vaccine antigens was assessed, 21 days after vaccination. The immunogenicity endpoints were the percentage of children and adolescents who achieved seroconversion, defined as a pre-vaccination hemagglutination inhibition (HI) titer of < 1:10 and a minimum 4-fold increase in post-vaccination HI antibody titer or with a pre-vaccination HI titer of ≥ 1:40 and a minimum 4-fold increase in post-vaccination HI antibody titer or with a pre-vaccination HI titer of ≥ 1:40 and a minimum 4-fold increase in post-vaccination HI antibody titer Study 1: NCT01992094

Table 7: Noninferiority of FLUCELVAX QUADRIVALENT relative to TIVc in adults 18 years of Age and Above—Per Protocol Analysis Set3 (Study 1)

<table>
<thead>
<tr>
<th>Vaccine Group</th>
<th>FLUCELVAX Quadrivalent N = 1250</th>
<th>TIV1c/TIV2c2 N = 635/ N = 639</th>
<th>Vaccine Group Ratio (95% CI)</th>
<th>Vaccine Group Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GMT (95% CI)</td>
<td>302.8 (281.8-325.5)</td>
<td>298.9 (270.3-310.5)</td>
<td>1.0 (0.9-1.1)</td>
</tr>
<tr>
<td></td>
<td>Seroconversion Rate1 (95% CI)</td>
<td>49.2% (46.4-52.0)</td>
<td>48.7% (44.7-52.6)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>GMT (95% CI)</td>
<td>372.3 (349.2-396.9)</td>
<td>378.4 (345.1-414.8)</td>
<td>1.0 (0.9-1.1)</td>
</tr>
<tr>
<td></td>
<td>Seroconversion Rate1 (95% CI)</td>
<td>38.3% (35.6-41.1)</td>
<td>35.6% (31.9-39.5)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>GMT (95% CI)</td>
<td>133.2 (125.3-141.7)</td>
<td>115.6 (106.4-126.6)</td>
<td>0.9 (0.8-1.0)</td>
</tr>
<tr>
<td></td>
<td>Seroconversion Rate1 (95% CI)</td>
<td>36.6% (33.9-39.3)</td>
<td>34.8% (31.3-38.7)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>GMT (95% CI)</td>
<td>177.2 (167.6-187.5)</td>
<td>164.0 (151.4-177.2)</td>
<td>0.9 (0.9-1.0)</td>
</tr>
<tr>
<td></td>
<td>Seroconversion Rate1 (95% CI)</td>
<td>39.8% (37.0-42.5)</td>
<td>35.4% (31.7-37.9)</td>
<td>-</td>
</tr>
</tbody>
</table>

1Comparisons were determined by the method of differences with respect to mean geometric mean titers (GMTs) of HI antibodies response and percentage of adults achieving seroconversion at 3 weeks following vaccination. The immunogenicity endpoints were geometric mean antibody titers (GMTs) of HI antibodies response and percentage of adults achieving seroconversion at 3 weeks following vaccination. The immunogenicity endpoints were the percentage of children and adolescents who achieved seroconversion, defined as a pre-vaccination hemagglutination inhibition (HI) titer of < 1:10 and a minimum 4-fold increase in post-vaccination HI antibody titer or with a pre-vaccination HI titer of ≥ 1:40 and a minimum 4-fold increase in post-vaccination HI antibody titer.

Abbreviations: VE = vaccine efficacy; GMT = geometric mean titer; CI = confidence interval.

1 Seroconversion rate = percentage of participants with either a pre-vaccination HI titer < 1:10 and post-vaccination HI titer ≥ 1:40 or with a pre-vaccination HI titer ≥ 1:40 and a minimum 4-fold increase in post-vaccination HI titer. Immunogenicity success criteria were met if the lower limit of the 95% confidence interval (CI) of the percentage of participants with HI titer ≥ 1:40 is ≥ 70%; and the lower limit of the 95% CI of the percentage of participants with seroconversion is ≥ 40%.

2 Per protocol set: All participants in Full Analysis Set, immunoeggensitivity analysis, who has correctly received the assigned vaccine, have no major protocol deviations leading to exclusion as defined prior to unblinding/analysis and are not excluded due to other reasons defined prior to unblinding or analysis.

3 Vaccine Group: (MENVEO, meningococcal (Groups A, C, Y, and W-135) oligosaccharide diphtheria CRM197 conjugate vaccine, GlaxoSmithKline Biologicals SA); children assigned to 2 doses received saline placebo as the second dose.

14.4 Immunogenicity in Children and Adolescents 4 through 17 years of age Immunogenicity of FLUCELVAX QUADRIVALENT was evaluated in children and adolescents 4 through 17 years of age in a randomized, double-blind, controlled study conducted in the US (Study 4). (See section 6.1) In this study, 1159 children and adolescents received FLUCELVAX QUADRIVALENT. In the per protocol set, the mean age of children and adolescents who received FLUCELVAX QUADRIVALENT was 9.8 years; 47% of children and adolescents were female and 54% of children and adolescents were Caucasian; 22% were black and 19% were Hispanics. The immune response to each of the vaccine antigens was assessed, 21 days after vaccination. The immunogenicity endpoints were the percentage of children and adolescents who achieved seroconversion, defined as a pre-vaccination hemagglutination inhibition (HI) titer of < 1:10 and a minimum 4-fold increase in serum HI titer, and percentage of children and adolescents with a post-vaccination HI titer ≥ 1:40. In children and adolescents receiving FLUCELVAX QUADRIVALENT, for all four influenza strains, the 95% LBCI seroconversion rates were ≥ 40% and the percentage of children and adolescents who achieved HI titer ≥ 1:40 post vaccination were ≥ 70% (95% LBCI). (See Table 8)
15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
FLUCELVAX QUADRIVALENT product presentations are listed in Table 9 below:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-filled Syringe</td>
<td>70461-320-03</td>
<td>0.5 mL single dose pre-filled syringe, package of 10 syringes per carton [NDC 70461-320-04]</td>
</tr>
<tr>
<td>Multi-dose Vial</td>
<td>70461-420-10</td>
<td>5 mL multi-dose vial, individually packaged in a carton [NDC 70461-420-11]</td>
</tr>
</tbody>
</table>

Store this product refrigerated at 2°C to 8°C (36°F to 46°F). Between uses, return the multi-dose vial to the recommended storage conditions. Do not freeze. Protect from light. Do not use after the expiration date.

17 PATIENT COUNSELING INFORMATION
Inform vaccine recipients of the potential benefits and risks of immunization with FLUCELVAX QUADRIVALENT.
Educate vaccine recipients regarding the potential side effects; clinicians should emphasize that (1) FLUCELVAX QUADRIVALENT contains non-infectious particles and cannot cause influenza and (2) FLUCELVAX QUADRIVALENT is intended to provide protection against illness due to influenza viruses only and cannot provide protection against other respiratory illnesses.
Instruct vaccine recipients to report adverse reactions to their healthcare provider.
Provide vaccine recipients with the Vaccine Information Statements which are required by the National Childhood Vaccine Injury Act of 1986. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Inform vaccine recipients that annual vaccination is recommended.
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Distributed by: Seqirus USA Inc. 25 Deforest Avenue, Summit, NJ 07901, USA
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