Introducing a flu shot that could reshape the way you think about flu protection

Influenza virus
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FLUCELVAX QUADRIVALENT® is an inactivated influenza 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 4 years of age and older.

Selected Important Safety Information
Contraindication
• Do not administer FLUCELVAX QUADRIVALENT to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine.1

Please see Important Safety Information throughout and accompanying US full Prescribing Information.
Introducing a flu shot that could reshape the way you think about flu protection

Indications and Usage for FLUCELVAX QUADRIVALENT® (Influenza Vaccine)

FLUCELVAX QUADRIVALENT® is an inactivated influenza 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 4 years of age and older.

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Influenza is a common, highly contagious infectious disease. Each year, between 5% and 20% of the US population are infected with the influenza virus. Unlike some other common respiratory illnesses, influenza can cause severe illness and life-threatening complications in many people. On average, more than 200,000 people are hospitalized each year for respiratory and heart condition illnesses associated with seasonal influenza virus infections.

To reduce mortality and morbidity resulting from influenza, the Advisory Committee on Immunization Practices recommends that all individuals in the United States aged 6 months and older receive an annual vaccination. This represents greater than 300 million individuals who should receive an annual vaccine. Despite issuing this recommendation in 2010, slightly fewer than half (47%) of individuals aged 6 months and older in the United States received an annual influenza vaccination during the 2014-2015 flu season.

In an analysis of 31 flu seasons between 1976 and 2007, estimates of annual flu-related deaths in the United States ranged from approximately 3000 to 49,000.

Between 2012 and 2015, there were 143 pediatric deaths on average during each flu season.

Up to 111 million workdays are lost due to influenza on an annual basis.

Approximately 90% of the children who died during the 2012-2013 flu season had not received a flu shot that season.
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 4 years of age and older.1 For children and adolescents 4 through 17 years of age, approval is based on the immune response elicited by FLUCELVAX QUADRIVALENT. Data demonstrating a decrease in influenza disease after vaccination of this age group with FLUCELVAX QUADRIVALENT are not available.

Warnings & Precautions
• Preventing and Managing Allergic Reactions: Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.1

Please see continued Selected Important Safety Information throughout and accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.
FLUCELVAX QUADRIVALENT (influenza vaccine) is made using the same modern cell culture technology as its predecessor, FLUCELVAX® (influenza vaccine). With cell culture technology, the vaccine is produced in sterile bioreactors, eliminating the need for antibiotics.

FLUCELVAX QUADRIVALENT is made in the USA. Our manufacturing facility in Holly Springs, North Carolina, was the first of its kind in the United States and was developed with support from the US government. Development of the technology and manufacturing facility that produces the vaccine was supported by the US government to help ensure that flu shots are available when needed.

A 21st-century flu shot

FLUCELVAX QUADRIVALENT (influenza vaccine) is made using the same modern cell culture technology as its predecessor, FLUCELVAX® (influenza vaccine). With cell culture technology, the vaccine is produced in sterile bioreactors, eliminating the need for antibiotics.

Selected Important Safety Information

Warnings & Precautions

• 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.

The change to using cells rather than eggs represented the first major development in influenza vaccine manufacturing technology since vaccine production began in the 1930s.

Cell culture-based influenza vaccine manufacturing does not depend on egg supply and has the potential to be scaled up for rapid production in response to outbreaks or pandemics. Cell culture is a proven technology that is also used to produce polio, smallpox, rubella, and chicken pox vaccines.

Please see continued Selected Important Safety Information throughout and accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.
Comparison of influenza vaccine manufacturing techniques

**CELL CULTURE-BASED INFLUENZA VACCINES**
- Use readily available bank of frozen characterized cells
- Grow virus in closed sterile bioreactors
- Manufacturing technology eliminates the need for the use of antibiotics
- Potential for rapid scale-up during outbreaks or pandemic

**EGG-BASED INFLUENZA VACCINES**
- Rely on egg availability. Supply may be affected by avian flu
- Grow virus in an open system
- Egg-based manufacturing may require use of antibiotics in the process
- Potentially limited flexibility to respond to market changes or demands

Building on a platform of influenza protection

FLUCELVAX QUADRIVALENT (influenza vaccine) is an evolution of FLUCELVAX. Because they are made in the same way and have overlapping compositions, the clinical efficacy of FLUCELVAX has been shown to be efficacious against influenza caused by vaccine-like strains (83.8%) and by all circulating influenza strains (69.5%).

Efficacy of FLUCELVAX (influenza vaccine) against culture-confirmed influenza

- 83.8% of viruses matched to those in the vaccine
- 69.5% of all influenza viruses

Selected Important Safety Information

**Warnings & Precautions**
- Altered Immunocompetence: After vaccination with FLUCELVAX QUADRIVALENT, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response.

Please see continued Selected Important Safety Information throughout and accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.
Demonstrated immunogenicity in children and adults

The immunogenicity of FLUCELVAX QUADRIVALENT was evaluated in 2 randomized, double-blind, controlled studies conducted in the United States in adults 18 years and older (Study 1) and children 4 through 17 years of age (Study 2). In Study 1, adults received FLUCELVAX QUADRIVALENT, TIV1c, or TIV2c. In Study 2, 1159 subjects received FLUCELVAX QUADRIVALENT. The immune response to each of the vaccines was assessed 21 days after vaccination. In adults aged 18 to 49 years, FLUCELVAX QUADRIVALENT was noninferior to comparator trivalent influenza vaccines for all 4 strains included in the vaccine, as assessed by ratios of hemagglutination inhibition (HI) geometric mean titers (GMTs) and differences in the percentage of subjects who achieved seroconversion 3 weeks postvaccination.

In children and adolescents aged 4 through 17 years who received FLUCELVAX QUADRIVALENT, the 95% lower bound confidence interval (LBCI) seroconversion rates were ≥40% and the percentage of subjects who achieved HI titer ≥1:40 postvaccination were ≥70% (95% LBCI).

<table>
<thead>
<tr>
<th>STRAIN</th>
<th>DIFFERENCE IN SEROCONVERSION RATE (FLUCELVAX QUADRIVALENT – TIV1c/TIV2c) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>-0.5% (-5.3, 4.2)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>-2.7% (-7.2, 1.8)</td>
</tr>
<tr>
<td>B1</td>
<td>-1.8% (-4.2, 2.8)</td>
</tr>
<tr>
<td>B2</td>
<td>-4.4% (-7.8, 0.2)</td>
</tr>
</tbody>
</table>

HI GMT ratios for TIV1c/TIV2c to FLUCELVAX QUADRIVALENT (influenza vaccine) in adults aged 18 years and older

<table>
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<th>VACCINE STRAIN</th>
<th>PERCENT</th>
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<tbody>
<tr>
<td>A/H1N1</td>
<td>1014</td>
</tr>
<tr>
<td>A/H3N2</td>
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</tr>
<tr>
<td>B1</td>
<td>1013</td>
</tr>
<tr>
<td>B2</td>
<td>1009</td>
</tr>
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</table>

The antibody response to influenza B strains contained in FLUCELVAX QUADRIVALENT was superior to the antibody responses after vaccination with TIVc containing an influenza B strain from the alternate lineage.

Selected Important Safety Information

Warnings & Precautions

- Limitations of Vaccine Effectiveness: Vaccination with FLUCELVAX QUADRIVALENT may not protect all vaccine recipients against influenza disease. Please see continued Selected Important Safety Information throughout and accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.

Vaccines may have an impact on the immune response to other vaccines that are given concurrently, especially those given within 2 weeks of each other. This immune response may be delayed by up to 2 weeks. In addition, the response to the seasonal influenza vaccine may wane with time and the immune response may be weaker in children and adolescents than in adults.
Well tolerated in children and adults

The safety of FLUCELVAX QUADRIVALENT was evaluated in 2 randomized, double-blind, controlled studies in which 5012 subjects (N = 2332 children 4 through 17 years of age and 2680 adults 18 years and older) received FLUCELVAX QUADRIVALENT or 1 of 2 comparator trivalent vaccines (TIV1c or TIV2c). The safety populations included all subjects who provided postvaccination symptom data in the form of a symptom diary card for 7 days following vaccination.1

Most common (≥10%) local and systemic adverse reactions observed within 7 days of vaccination with FLUCELVAX QUADRIVALENT1

Incidence of serious adverse events reported within 6 months of vaccination with FLUCELVAX QUADRIVALENT (influenza vaccine)1

<table>
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<th>Age Group</th>
<th>Local Reactions</th>
<th>Systemic Reactions</th>
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<tr>
<td>Adults 18 Years and Older</td>
<td>Injection site pain (34%)</td>
<td>Headache (14%)</td>
</tr>
<tr>
<td>Children and Adolescents Aged 4 to 17 Years</td>
<td>Injection site pain (58%)</td>
<td>Headache (22%)</td>
</tr>
<tr>
<td>Adults 65 Years and Older</td>
<td>Injection site pain (21%)</td>
<td>Headache (9%)</td>
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In children who received a second dose of FLUCELVAX QUADRIVALENT (ex. children aged 4 to 8 years), the incidence of adverse events was generally lower following the second dose.1

The safety of FLUCELVAX QUADRIVALENT is relevant to that of FLUCELVAX because they are both made by cell culture technology and have overlapping compositions.1

The safety of FLUCELVAX has a similar safety profile to that of traditional egg-based influenza vaccines. The safety of FLUCELVAX is relevant to that of FLUCELVAX QUADRIVALENT because they are both made by cell culture technology and have overlapping compositions.1

A history of flu prevention

The most common (≥10%) local and systemic solicited adverse reactions in subjects receiving FLUCELVAX were1

- Adults 18 to 64 years of age— injection site pain (28%), injection site erythema (13%), headache (16%), fatigue (12%), myalgia (11%), malaise (10%)
- Adults 65 years and older— injection site erythema (10%), fatigue (11%), headache (10%), malaise (10%)
- Children 4 through 8 years of age — injection site pain (29%), injection site erythema (11%), fatigue (10%), malaise (12%), loss of appetite (10%)
- Children and adolescents 9 through 17 years — injection site pain (24%), myalgia (15%), headache (14%), injection site erythema (14%)

Please see continued Selected Important Safety Information throughout and accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.

“Some of the SAEs were assessed as being related to study vaccine.11

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**Important Safety Information**

**Contraindication**

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

**Adverse Events**

- **Syncope**:
  - After vaccination with FLUCELVAX QUADRIVALENT, syncope can be managed by maintaining a supine or Trendelenburg position.
  - Syncope can be associated with transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements.

**Pain and Injection Site Reactions**

The most common (≥10%) local and systemic reactions in adults 18-64 years of age were injection site pain (45.4%), headache (18.7%), fatigue (17.8%), and myalgia (15.4%); injection site erythema (13.4%), and induration (11.6%).

**Reactions in Children**

In children 6 through 8 years of age were injection site (46%), injection site erythema (18%), and change in eating habits (10%).

**Syncope**

Syncope can be associated with transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements.

**Pain and Injection Site Reactions**

The most common (≥10%) local and systemic reactions in children 6 through 8 years of age were pain at the injection site (58%), injection site induration (13%), and change in eating habits (10%).

Please see accompanying full Prescribing Information for FLUCELVAX QUADRIVALENT.
FLUCELVAX QUADRIVALENT—It’s time to reshape the way you think about flu shots.

• Approved for individuals aged 4 years and older
• Made using the same proven technology as FLUCELVAX (influenza vaccine), the first FDA-approved influenza vaccine made with cell culture technology
• Contains the same flu strains as trivalent vaccines, plus one additional strain
• Offers similar immunogenicity and safety as comparable trivalent influenza vaccines
• Manufacturing technology eliminates the need for the use of antibiotics
• Available in prefilled syringes that are preservative and latex free

Indications and Usage
FLUCELVAX QUADRIVALENT is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. FLUCELVAX QUADRIVALENT is approved for use in persons 4 years of age and older. For children and adolescents 4 through 17 years of age, approval is based on the immune response elicited by FLUCELVAX QUADRIVALENT. Data demonstrating a decrease in influenza disease after vaccination of this age group with FLUCELVAX QUADRIVALENT are not available.

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For more information, please visit www.flucelvax.com

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