Influenza Vaccine
FLUCELVAX®
QUADRIVALENT

REAL-WORLD EVIDENCE (RWE) STUDIES SUPPORT THE CLINICAL EFFECTIVENESS OF FLUCELVAX® QUADRIVALENT (Influenza Vaccine)[1-11]

Because influenza varies each year, look to both clinical trials and RWE when choosing an influenza vaccine[12,13]

In clinical trials:

- FLUCELVAX QUADRIVALENT demonstrated efficacy in children and adolescents 2 through 17 years
- FLUCELVAX QUADRIVALENT was proven noninferior to a US-licensed comparator influenza vaccine based on immunogenicity and seroconversion for patients 6 months through 3 years
- FLUCELVAX QUADRIVALENT was proven noninferior to FLUCELVAX® (Influenza Vaccine) based on immunogenicity and seroconversion for patients 4 years and older
- FLUCELVAX demonstrated efficacy against culture-confirmed influenza in those 18 through 49 years*

*The efficacy data of FLUCELVAX are relevant to FLUCELVAX QUADRIVALENT, as both vaccines are manufactured using the same process and have overlapping compositions.

FLUCELVAX® QUADRIVALENT (Influenza Vaccine)
IMPORTANT SAFETY INFORMATION

INDICATION 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 types B contained in the vaccine. FLUCELVAX QUADRIVALENT is approved for use in persons 6 months of age and older.

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

Please see Important Safety Information throughout and the accompanying full US Prescribing Information for FLUCELVAX QUADRIVALENT.

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FLUCELVAX® QUADRIVALENT (Influenza Vaccine) vs standard-dose, egg-based influenza vaccines

The outcomes reported in these publications contain information not included in the Prescribing Information.

These studies provide data across 3 US influenza seasons with different study designs, outcomes, and study limitations comparing the relative vaccine effectiveness (rVE) of FLUCELVAX QUADRIVALENT compared to traditional, egg-based influenza vaccines.[1-11]

In seasons where egg adaptation occurs, studies suggest FLUCELVAX QUADRIVALENT has the potential to be more effective than traditional, egg-based vaccines.[1-11]

End Points	Study Results	Season(s)	Study Design	Key Limitations
	Favors egg-based influenza vaccines ← → Favors FLUCELVAX QIV -30 -20 -10 0 10 20 30 40 50			
8% **fewer laboratory-confirmed Influenza A illnesses*[1]** (rVE 8%; 95% CI -10, 23)		2017-2018	Retrospective cohort study of over **1 million persons** 4-64 years old in the US†	• Low proportion of vaccinees received QIVc, limiting study power • Potential for bias if providers preferentially gave either vaccine to higher-risk individuals
40% **fewer laboratory-confirmed Influenza B illnesses*[1]** (rVE 39.6%; 95% CI 27.9, 49.3)		2017-2018	Retrospective cohort study of **888,233 persons** 4-64 years old in the US†	• Low proportion of vaccinees received QIVc, limiting study power • Potential for bias if providers preferentially gave either vaccine to higher-risk individuals
No difference in the relative VE for laboratory-confirmed influenza[2] (rVE 0%; 95% CI -30, 20)‡		2017-2018	Test-negative case-control study of **1508 DoD healthcare beneficiaries** ≥6 months old in the US†	• Due to a limited supply of vaccine, the DoD asked persons ≥9 years to receive QIVc • Results did not account for comorbidities and health status
15% **fewer laboratory-confirmed influenza hospitalizations[3]** (rVE 15%; 95% CI -26, 43)		2017-2018	Test-negative case-control study of **5,471 persons** ≥4 years in the US†	• Results did not account for all residual confounding (eg, frailty) • Selection bias in hospitalizations and testing
36% **fewer influenza-like illnesses within a primary care setting[4]** (rVE 36.2%; 95% CI 26.1, 44.9)		2017-2018	Retrospective cohort study of **over 1.3 million persons** ≥4 years in the US	• Results were not adjusted by unmeasurable confounders • Inability to reliably estimate absolute influenza VE from the ambulatory EMR dataset
14% **fewer influenza-related hospitalizations or ER visits[5]** (rVE 14.4%; 95% CI 8.8, 19.6)		2017-2018	Retrospective cohort study of **over 3 million persons** 4-64 years old in the US	• Results were not adjusted by unmeasurable confounders • Findings may not be representative of uninsured, Medicaid, or Medicare populations
11% **fewer influenza-related hospital encounters[6]** (rVE 11%; 95% CI 7.9, 14)		2017-2018	Retrospective cohort study of **over 2.5 million adults** ≥65 years in the US	• Potential for residual confounding • Medicare claims may not be representative of private or uninsured populations
3% **fewer influenza-related hospitalizations or ER visits[7]** (rVE 2.5%; 95% CI -2.4, 7.3)		2018-2019	Retrospective cohort study of **over 2.2 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
7% **fewer influenza-related hospitalizations or ER visits[8]** (rVE 6.5%; 95% CI 0.1, 12.5)		2018-2019	Retrospective cohort study of **over 3.7 million persons** 4-64 years old in the US	• Results were not adjusted by unmeasurable confounders • Findings may not be representative of uninsured, Medicaid, or Medicare populations
8% **fewer influenza-related medical encounters[9]** (rVE 7.6%; 95% CI 6.5, 8.6)		2018-2019	Retrospective cohort study of **over 10.1 million persons** ≥4 years in the US	• Analyses did not specifically adjust for frailty • Unmeasured confounding is a potential source of bias
3% **fewer influenza-related hospital encounters[10]** (rVE 2.8%; 95% CI -2.8, 8.2)		2019-2020	Retrospective cohort study of **over 2.4 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
5% **fewer influenza-related hospitalizations or ER visits[11]** (rVE 5.3%; 95% CI 0.5, 9.9)		2019-2020	Retrospective study of **over 5 million persons** 4-64 years old in the US	• Potential for unmeasured confounders • Lack of laboratory confirmation

*These results are from the same study. The rVE for influenza A compared QIVc to both TIVe and QIVe and the rVE for influenza B compared QIVc to TIVe only
†There was also an unvaccinated arm in this study
‡rVE calculated as (1-adjusted odds ratio) x 100

CI=confidence interval; DoD=Department of Defense; QIVc=cell-based, quadrivalent influenza vaccine; QIVe=egg-based, quadrivalent influenza vaccine; rVE=relative vaccine effectiveness; TIVe=egg-based, trivalent influenza vaccine; VE=vaccine effectiveness

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.

WARNINGS AND PRECAUTIONS (continued)

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

Please see Important Safety Information throughout and the accompanying full US Prescribing Information for FLUCELVAX QUADRIVALENT.

RWE STUDIES SUPPORT THE CLINICAL EFFECTIVENESS OF **FLUCELVAX® QUADRIVALENT** (Influenza Vaccine)*[1-11]

Influenza Vaccine
FLUCELVAX®
QUADRIVALENT

A cell-based flu vaccine designed to produce an exact match to the WHO-selected strains.[15-17]

When considering influenza vaccine options for those 6 months and older, consider FLUCELVAX QUADRIVALENT.[14]

*The RWE studies of FLUCELVAX QUADRIVALENT were conducted in patients 4 years and older because that was the age indication at the time the studies were being conducted. The FDA has since approved FLUCELVAX QUADRIVALENT for patients 6 months and older in October 2021.

WHO=World Health Organization

FLUCELVAX® QUADRIVALENT (Influenza Vaccine) IMPORTANT SAFETY INFORMATION

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CONTRAINDICATIONS

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

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.

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

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.

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

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

ADVERSE REACTIONS

In children 6 months through 3 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (27.9%), erythema (25.8%), induration (17.3%) and ecchymosis (10.7%). The most common systemic adverse reactions were irritability (27.9%), sleepiness (26.9%), diarrhea (17.9%) and change of eating habits (17.4%).

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 reactions 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 reactions were headache (18.1%) and fatigue (17.0%).

In adults 18 through 64 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (45.4%), erythema (13.4%) and induration (11.6%). The most common systemic adverse reactions were headache (18.7%), fatigue (17.8%) and myalgia (15.4%).

In adults ≥65 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were pain (21.6%) and erythema (11.9%).

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

Before administration, please see the full US Prescribing Information for FLUCELVAX QUADRIVALENT.

FLUCELVAX ® QUADRIVALENT is a registered trademark of Seqirus UK Limited or its affiliates.

REFERENCES: 1. Klein NP, et al. *PLoS ONE*. 2020;15(2):e0229279. **2.** DeMarcus L. et al. *Vaccine*. 2019;37(30):4015-4021. **3.** Bruxvoort KJ, et al. *Vaccine*. 2019;37(39):5807-5811. **4.** Boikos C, et al. *Clin Infect Dis*. 2020;ciaa371. **5.** Divino V, et al. *Vaccine*. 2020;38(40):6334-6343. **6.** Izurieta HS, et al. *J Infect Dis*. 2019;220(8):1255-1264. **7.** Izurieta HS, et al. *J Infect Dis*. 2020;222(2):278-287. **8.** Krishnarajah G, et al. *Vaccines (Basel)*. 2021;9(2):80. **9.** Boikos C, et al. *Clin Infect Dis*. 2021;ciaa1944. **10.** Izurieta HS, et al. *Clin Infect Dis*. 2020;19:ciaa1727. **11.** Divino V, et al. *Open Forum Infect Dis*. 2021;9(1):ofab604. **12.** CDC. How flu vaccine effectiveness and efficacy are measured. Accessed April 22, 2021. https://www.cdc.gov/flu/vaccines-work/effectivenessqa.htm **13.** Katkade VB, et al. *J Multidiscip Healthc*. 2018;11:295-304. **14.** FLUCELVAX QUADRIVALENT. Package insert. Seqirus Inc; 2021. **15.** Rajaram S, et al. *Ther Adv Vaccines Immunother*. 2020;8:2515135520908121. **16.** CDC. Cell-based flu vaccines. Accessed August 3, 2021. https://www.cdc.gov/flu/prevent/cell-based.htm **17.** Mabrouk T, et al. *Dev Biol*. 2002;110:125-134.

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