FLUAD® QUADRIVALENT
influenza vaccine, adjuvanted

20+ years of real-world evidence (RWE) studies support the clinical effectiveness of FLUAD® (influenza vaccine, adjuvanted) in adults 65+[1-12]

Because influenza varies each year, look to both clinical trial and RWE data when choosing an influenza vaccine.[13,14]

In immunogenicity clinical trials[15]:

- FLUAD met non-inferiority criteria compared to a non-adjuvanted, standard-dose influenza vaccine.
- FLUAD® QUADRIVALENT met non-inferiority criteria compared to a non-flu comparator vaccine.

The trivalent formulation was approved in the US in 2015 and Europe in 1997. The quadrivalent formulation was approved in the US in 2020 and is the only formulation available now.

INDICATION AND USAGE

FLUAD QUADRIVALENT is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and types B contained in the vaccine. FLUAD QUADRIVALENT is approved for use in persons 65 years of age and older.

This indication is approved under accelerated approval based on the immune response elicited by FLUAD QUADRIVALENT.

CONTRAINDICATIONS

Do not administer FLUAD QUADRIVALENT to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine, including egg protein, or to a previous influenza vaccine.

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

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FLUAD® (Influenza Vaccine, Adjuvanted) vs a high-dose influenza vaccine

The RWE studies for FLUAD are relevant to FLUAD® QUADRIVALENT because both products are manufactured using the same process and have overlapping compositions. The outcomes reported in these publications contain information not included in the Prescribing Information.

RWE studies from across 4 US influenza seasons with different study designs, outcomes, and study limitations assessed the relative vaccine effectiveness of FLUAD compared to a high-dose influenza vaccine.[1-5,11,12]

End Points	Study Results	Season(s)	Study Design	Key Limitations
	Favors a high-dose influenza vaccine ◀ ▶ Favors FLUAD -30 -20 -10 0 10 20 30			
1.6% **fewer influenza-related hospitalization encounters**[1] (rVE 1.6%; 95% CI -1.6, 4.8)		**1 season** (2019-2020)	Retrospective cohort study of **over 9.7 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
3% **fewer influenza-related hospitalization encounters**[2] (rVE 3%; 95% CI 0, 6.1)		**1 season** (2018-2019)	Retrospective cohort study of **over 10 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
2% **fewer influenza-related hospitalizations and ER visits**[11] (rVE 2%; 95% CI -3.7, 7.3)		**1 season** (2018-2019)	Retrospective cohort study of **over 2.2 million adults** ≥65 years from the US	• Results were not adjusted by unmeasurable confounders • Lack of laboratory confirmation
6.6% **fewer influenza-related office visits**[11] (rVE 6.6%; 95% CI 2.7, 10.3)				
6.9% **fewer influenza-related medical encounters**[3] (rVE 6.9%; 95% CI 3.1, 10.6)		**1 season** (2018-2019)	Retrospective cohort study of **over 4.8 million adults** ≥65 years from the US	• Results were not adjusted by unmeasurable confounders • Lack of laboratory confirmation
7.7% **fewer influenza-related medical encounters**[3] (rVE 7.7%; 95% CI 2.3, 12.8)		**1 season** (2017-2018)	Retrospective cohort study of **over 3.9 million adults** ≥65 years from the US	• Results were not adjusted by unmeasurable confounders • Lack of laboratory confirmation
-5.3% **fewer influenza-related hospitalization encounters**[4] (rVE -5.3%; 95% CI -7.3, -3.3)		**1 season** (2017-2018)	Retrospective cohort study of **9.9 million adults** ≥65 years in the US	• Potential for residual confounding • Medicare claims may not be representative of private or uninsured populations
16.6% **fewer influenza-related office visits**[5] (rVE 16.6%; 95% CI 10.8, 22)		**1 season** (2017-2018)	Retrospective cohort study of **1.5 million adults** ≥65 years in the US	• Results were not adjusted by unmeasurable and unobservable confounders • Stringent influenza-related office visit definition
3.2% **fewer influenza-related hospitalizations and ER visits**[5] (rVE 3.2%; 95% CI -2.7, 8.9)				
2.4% **fewer other respiratory hospitalizations and ER visits**[5] (rVE 2.4%; 95% CI 0.7, 4)				
-12% **fewer respiratory-related hospitalizations**[12] (rVE -12%; 95% CI -20, -3.3)		**2 consecutive seasons** (2016-2017 through 2017-2018)	Retrospective cohort study of over **2.1 million adults** ≥65 years in the US	• Results were unable to be adjusted for unobservable confounders • Uneven cohort sizes between the seasons made results heavily influenced by 2017-2018 season

CI=confidence interval; ER=emergency room; rVE=relative vaccine effectiveness

WARNINGS AND PRECAUTIONS

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUAD 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 FLUAD QUADRIVALENT.

FLUAD® (Influenza Vaccine, Adjuvanted) **vs standard-dose influenza vaccines**

The RWE studies for FLUAD are relevant to FLUAD® QUADRIVALENT because both products are manufactured using the same process and have overlapping compositions. The outcomes reported in these publications contain information not included in the Prescribing Information.

RWE studies from across 18 influenza seasons with different study designs, outcomes, and study limitations assessed the relative vaccine effectiveness of FLUAD compared to standard-dose influenza vaccines.[1-10]

End Points	Study Results	Season(s)	Study Design	Key Limitations
	Favors a standard-dose influenza vaccine ← → Favors FLUAD -10 0 10 20 30 40 50 60 70 80 90			
8.2% **fewer influenza hospitalization encounters**[1] (rVE 8.2%; 95% CI 4.2-12)		**1 season** (2019-2020)	Retrospective cohort study of **over 4.1 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
7.7% **fewer influenza hospitalization encounters**[2] rVE 7.7%; 95% CI 3.9-11.14)		**1 season** (2018-2019)	Retrospective cohort study of **over 3.5 million adults** ≥65 years from the US	• Potential for residual confounding • Lack of laboratory confirmation
27.8% **fewer influenza-related medical encounters**[3] (rVE 27.8%; 95% CI 25.7-29.9)		**1 season** (2018-2019)	Retrospective cohort study of **over 1.9 million adults** ≥65 years from the US	• Results were not adjusted by unmeasurable confounders • Lack of laboratory confirmation
18.2% **fewer influenza-related medical encounters**[3] (rVE 18.2%; 95% CI 15.8-20.5)		**1 season** (2017-2018)	Retrospective cohort study of **over 1.4 million adults** ≥65 years from the US	• Results were not adjusted by unmeasurable confounders • Lack of laboratory confirmation
3.9% **fewer influenza-related hospitalization encounters**[4] (rVE 3.9%; 95% CI 1.4-6.3)		**1 season** (2017-2018)	Retrospective cohort study of **over 3.2 million adults** ≥65 years from the US	• Potential for residual confounding • Medicare claims may not be representative of private or uninsured populations
36.3% **fewer influenza-related office visits**[5] (rVE 36.3%; 95% CI 31-41.2) **8.6%** **fewer influenza-related hospitalizations or ER visits**[5] (rVE 8.6%; 95% CI 1.2-15.6) **4%** **fewer cardio-respiratory hospitalizations or ER visits**[5] (rVE 4%; 95% CI 1.9-6.2)		**1 season** (2017-2018)	Retrospective cohort study of **446,600 adults** ≥65 years from the US	• Results were not adjusted by unmeasurable and unobservable confounders • Stringent influenza-related office visit definition
6% **fewer all-cause hospitalizations**[6] (rVE 6%; 95% CI 1-11)		**1 season** (2016-2017)	Prospective, randomized study of **823 nursing homes** housing **50,012** eligible residents in the US	• Study population may not represent US older adults • Lower frequency of events
33% **fewer hospitalizations for pneumonia**[7] (rVE 33%; 95% CI 25-41)		**6 consecutive seasons** (2011-2012 through 2016-2017)	Retrospective cohort study of **479,397 adults** ≥65 years from Italy	• Lack of unvaccinated control group • Lack of laboratory confirmation
63% **fewer laboratory-confirmed influenza illnesses**[8] (rVE 63%; 95% CI 4–86)		**1 season** (2011-2012)	Prospective, community-based, case-control study of **227 adults** ≥65 years from Canada	• Small study population • Low numbers prevented the evaluation of hospitalizations
25% **fewer influenza or pneumonia-related hospitalizations**[9] (rVE 25%; 95% CI 2–43)		**3 consecutive seasons** (2006-2007 through 2008-2009)	Prospective, observational, population-based cohort study of **107,661 adults** ≥65 years from Italy	• Underestimated rVE as FLUAD subjects were more frail • Results did not account for all the residual confounding
39% **fewer hospitalizations for pneumonia and cerebrovascular and/or cardiovascular events**[10] (rVE 39%; 95% CI 4–61)		**15 consecutive seasons** (2001-2002 through 2016-2017)	Retrospective, case-controlled study of **43,000 vaccine-naive adults** ≥65 years from Italy	• Underutilization of laboratory influenza diagnostics • Lower frequency of events

CI=confidence interval; ER=emergency room; rVE=relative vaccine effectiveness

WARNINGS AND PRECAUTIONS

The immune response to FLUAD QUADRIVALENT in immunocompromised persons, including individuals receiving immunosuppressive therapy, may be lower than in immunocompetent individuals.

WARNINGS AND PRECAUTIONS (continued)

Syncope (fainting) may occur in association with administration of injectable vaccines including FLUAD QUADRIVALENT. Ensure procedures are in place to avoid injury from falling associated with syncope.

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

20+ years of real-world evidence (RWE) studies support the clinical effectiveness of FLUAD® (influenza vaccine, adjuvanted) in adults 65+[1-12]

FLUAD® QUADRIVALENT influenza vaccine, adjuvanted

Adjuvanted to help prevent seasonal influenza in adults 65+[15]

Designed to strengthen, broaden, and lengthen the duration of the immune response[16-18]

FLUAD® QUADRIVALENT (Influenza Vaccine, Adjuvanted) INDICATION and IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Do not administer FLUAD QUADRIVALENT to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine, including egg protein, or to a previous influenza vaccine.

WARNINGS AND PRECAUTIONS

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUAD 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.

The immune response to FLUAD QUADRIVALENT in immunocompromised persons, including individuals receiving immunosuppressive therapy, may be lower than in immunocompetent individuals.

Syncope (fainting) may occur in association with administration of injectable vaccines including FLUAD QUADRIVALENT. Ensure procedures are in place to avoid injury from falling associated with syncope.

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

ADVERSE REACTIONS

The most common (≥10%) local and systemic reactions in elderly subjects 65 years of age and older were injection site pain (16.3%), headache (10.8%) and fatigue (10.5%).

To report SUSPECTED ADVERSE REACTIONS, contact Seqirus USA Inc. 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 FLUAD QUADRIVALENT.

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

REFERENCES: 1. Izurieta HS, et al. *Clin Infect Dis*. 2020;ciaa1727. **2.** Izurieta HS, et al. *J Infect Dis*. 2020;222:278-287. **3.** Boikos C, et al. *Clin Infect Dis*. 2021;ciab152. **4.** Izurieta HS, et al. *J Infect Dis*. 2019;220:1255-1264. **5.** Pelton SI, et al. *Vaccines (Basel)*. 2020;8(3):E446. **6.** McConeghy KW, et al. *Clin Infect Dis*. 2020;ciaa1233. **7.** Cocchio S, et al. *Vaccines*. 2020;8(3):344. **8.** Van Buynder PG, et al. *Vaccine*. 2013;31(51):6122-6128. **9.** Mannino S, et al. *Am J Epidemiol*. 2012;176(6):527-533. **10.** Lapi F, et al. *Expert Rev Vaccines*. 2019;18(6):663-670. **11.** Pelton SI, et al. *Vaccine*. 2021;39(17):2396-2407. **12.** van Aalst R, et al. *Vaccine*. 2020;38(2):372-379. **13.** CDC. How flu vaccine effectiveness and efficacy are measured. Accessed April 22, 2021. https://www.cdc.gov/flu/vaccines-work/effectivenessqa.htm **14.** Katkade VB, et al. *J Multidiscip Healthc*. 2018;11:295-304. **15.** FLUAD QUADRIVALENT. Package insert. Seqirus Inc; 2021. **16.** O'Hagan DT, et al. *Vaccine*. 2012;30(29):4341-4348. **17.** O'Hagan DT, et al. *Expert Rev Vaccines*. 2013;12(1):13-30. **18.** Banzhoff A, et al. *Influenza Other Respir Viruses*. 2008;2(6):243-249.

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