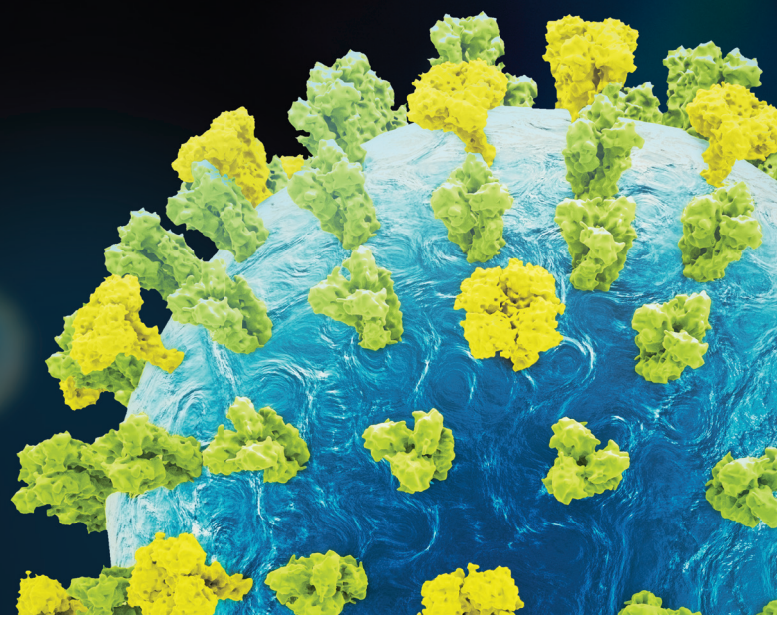
Adjuvanted to help prevent seasonal influenza in adults 65+[1]

FLUAD® QUADRIVALENT
influenza vaccine, adjuvanted

Designed to strengthen, broaden, and lengthen the duration of the immune response[2-4]



Learn more at fluad.com

For more information, please see Important Safety Information below and the Brief Summary on adjacent page.

INDICATION and IMPORTANT SAFETY INFORMATION

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.

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. FLUAD QUADRIVALENT. Package insert. Seqirus Inc; 2021. **2.** O'Hagan DT, Ott GS, De Gregorio E, Seubert A. The mechanism of action of MF59—an innately attractive adjuvant formulation. *Vaccine.* 2012;30(29):4341-4348. doi:10.1016/j.vaccine.2011.09.061 **3.** O'Hagan DT, Ott GS, Nest GV, Rappuoli R, Del Giudice G. The history of MF59® adjuvant: a phoenix that arose from the ashes. *Expert Rev Vaccines.* 2013;12(1):13-30. doi:10.1586/erv.12.140 **4.** Banzhoff A, Pellegrini M, Del Giudice G, Fragapane E, Groth N, Podda A. MF59-adjuvanted vaccines for seasonal and pandemic influenza prophylaxis. *Influenza Other Respir Viruses.* 2008;2(6):243-249. doi:10.1111/j.1750-2659.2008.00059.x

Seqirus™
A CSL COMPANY

FLUAD® QUADRIVALENT (Influenza Vaccine, Adjuvanted)
Injectable Emulsion for Intramuscular Use
2021-2022 Formula

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Consult the full US Prescribing Information for complete product information.

INDICATIONS 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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

For intramuscular injection only.

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

Guillain-Barré Syndrome: 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. The 1976 swine influenza vaccine was associated with an elevated risk of GBS. *[see Reference (1)]* Evidence for a causal relationship of GBS with other influenza vaccines is inconclusive; if an excess risk exists, it is probably slightly more than 1 additional case per 1 million persons vaccinated.

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

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

Syncope: 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.

Limitations of Vaccine Effectiveness: 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%).

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

The safety of FLUAD QUADRIVALENT was evaluated in two clinical studies in 4269 elderly subjects 65 years of age and older. Study 1 (NCT02587221) was a multi-center, randomized, observer-blind, non-influenza comparator-controlled efficacy and safety study conducted in 12 countries during the 2016-2017 Northern Hemisphere and 2017 Southern Hemisphere seasons. In this study, 3381 subjects received FLUAD QUADRIVALENT and 3380 subjects received a US-licensed non-influenza comparator vaccine (Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Boostrix® [GlaxoSmithKline Biologicals]).

The mean age of subjects at enrollment was 72 years, 62% were female, 48% White, 34% Asian, 16% Other, 2% American Indian/Alaska Native, and 18% of Hispanic/Latino ethnicity.

Solicited local and systemic adverse reactions were collected for 7 days after vaccination in a subset of 665 subjects who received FLUAD QUADRIVALENT and 667 subjects who received the comparator vaccine. The percentages of subjects reporting solicited local adverse reactions are presented in Table 1a and systemic adverse reactions are presented in Table 1b. Onset usually occurred within the first 2 days after vaccination. The majority of solicited reactions resolved within 3 days.

Table 1a. Percentages of Subjects Reporting Solicited Local Adverse Reactions[a] in the Solicited Safety Population[b] within 7 Days of Vaccination (Study 1)

Local (Injection site) Reactions[c]	FLUAD QUADRIVALENT N=595-659	Non-Influenza Comparator Vaccine N=607-664
Injection site pain	16.3	11.2
Erythema ≥25mm	3.8	1.8
Induration ≥25mm	4.0	2.6
Ecchymosis ≥25mm	0.5	0.7

Study 1: NCT02587221
Abbreviation: N=number of subjects with solicited safety data
Non-Influenza Comparator Vaccine = combined Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Boostrix® (GlaxoSmithKline Biologicals)
[a] All solicited local adverse events reported within 7 days of vaccination are included
[b] Solicited Safety Population: all subjects in the exposed population who received a study vaccine and provided post-vaccination solicited safety data
[c] Severe reactions of each type were reported in 1.1% or fewer subjects receiving FLUAD QUADRIVALENT; severe reactions of each type were also reported in the comparator group at similar percentages. Severe definitions: Erythema, Induration and Ecchymosis = >100 mm diameter; Injection site pain = prevents daily activity.

Table 1b. Percentages of Subjects Reporting Solicited Systemic Adverse Reactions[a] in the Solicited Safety Population[b] within 7 Days of Vaccination (Study 1)

Systemic Reactions[c]	FLUAD QUADRIVALENT N=595-659	Non-Influenza Comparator Vaccine N=607-664
Headache	10.8	8.3
Fatigue	10.5	8.8
Myalgia	7.7	6.1
Arthralgia	7.3	6.6
Chills	5.0	3.9
Diarrhea	4.1	3.0
Nausea	3.8	2.3
Loss of appetite	3.6	3.6
Fever ≥100.4°F (38°C)	1.7	1.2
Vomiting	0.8	1.1

Study 1: NCT02587221
Abbreviation: N=number of subjects with solicited safety data
Non-Influenza Comparator Vaccine = combined Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Boostrix® (GlaxoSmithKline Biologicals)
[a] All solicited systemic adverse events reported within 7 days of vaccination are included
[b] Solicited Safety Population: all subjects in the exposed population who received a study vaccine and provided post-vaccination solicited safety data
[c] Severe reactions of each type were reported in 1.1% or fewer subjects receiving FLUAD QUADRIVALENT; severe reactions of each type were also reported in the comparator group at similar percentages. Severe definitions: Nausea, Fatigue, Myalgia, Arthralgia, Headache, and Chills = prevents daily activity; Loss of appetite = not eating at all; Vomiting = 6 or more times in 24 hours or requires intravenous hydration; Diarrhea = 6 or more loose stools in 24 hours or requires intravenous hydration; Fever = ≥102.2°F (39°C).

Unsolicited adverse events (AEs) were collected for all subjects for 21 days after vaccination. Related unsolicited AEs were reported by 303 (9.0%) and by 261 (7.7%) of the subjects for FLUAD QUADRIVALENT and Boostrix, respectively. For FLUAD QUADRIVALENT, injection site pain and influenza-like illness were the only unsolicited adverse reactions reported in ≥ 1% of subjects (1.7% and 1.5%, respectively).

Serious adverse events (SAEs) and potentially immune-mediated adverse events of special interest (AESIs) were collected up to 366 days after vaccination. SAEs were reported by 238 (7.0%) FLUAD QUADRIVALENT recipients and 234 (6.9%) comparator recipients. There were no SAEs, AESIs or deaths in this study that were related to FLUAD QUADRIVALENT.

Study 2 (NCT03314662) was a multicenter, randomized, double-blind, comparator-controlled study conducted during the 2017-18 Northern Hemisphere influenza season. In this study, 888 subjects received FLUAD QUADRIVALENT, 444 subjects received the licensed adjuvanted trivalent vaccine (aTIV-1 - FLUAD® (trivalent formulation)) and 444 subjects received an adjuvanted trivalent influenza vaccine with an alternate B strain (aTIV-2).

The mean age of subjects at enrollment who received FLUAD QUADRIVALENT was 72.5 years. Female subjects represented 56.6% of the study population and the racial distribution of subjects was 91.6% Caucasian, 7.0% Black or African American, and ≤ 1% each for Asian, Native Hawaiian or Pacific Islander, American Indian or Alaska Native or Other.

Solicited local and systemic adverse reactions reported within 7 days after vaccination were similar to those reported for Study 1. Unsolicited AEs were collected for 21 days after vaccination. Related unsolicited AEs were reported by 39 (4.4%) and by 17-19 (3.8%-4.3%) of subjects administered FLUAD QUADRIVALENT or aTIV, respectively. For FLUAD QUADRIVALENT, injection site bruising (1.0%) was the only unsolicited adverse reaction reported in ≥ 1% of subjects.

Serious AEs and AESIs were collected up to 181 days after vaccination. Within 6 months after vaccination, 37 (4.2%) FLUAD QUADRIVALENT recipients and 18-28 (4.1%-6.3%) aTIV recipients experienced an SAE. There were no SAEs, AESIs or deaths in this study that were related to the study vaccine. There were no AEs leading to withdrawal from the study.

Postmarketing Experience: There are no postmarketing data available for FLUAD QUADRIVALENT. However, the postmarketing experience with FLUAD (trivalent formulation) is relevant to FLUAD QUADRIVALENT because both vaccines are manufactured using the same process and have overlapping compositions.

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.

Blood and lymphatic system disorders: Thrombocytopenia (some cases were severe with platelet counts less than 5,000 per mm^3), lymphadenopathy

General disorders and administration site conditions: Extensive swelling of injected limb lasting more than one week, injection site cellulitis-like reactions (some cases of swelling, pain, and redness extending more than 10 cm and lasting more than 1 week)

Immune system disorders: Allergic reactions including anaphylactic shock, anaphylaxis, and angioedema

Musculoskeletal and connective tissue disorders: Muscular weakness

Nervous systems disorders: Encephalomyelitis, Guillain-Barré Syndrome, convulsions, neuritis, neuralgia, parasthesia, syncope, presyncope

Skin and subcutaneous tissue disorders: Generalized skin reactions including erythema multiforme, urticaria, pruritus or nonspecific rash

Vascular disorders: Vasculitis, renal vasculitis

DRUG INTERACTIONS

Concomitant Use With Other Vaccines: No clinical data on concomitant administration of FLUAD QUADRIVALENT with other vaccines is available.

If FLUAD QUADRIVALENT is given at the same time as other injectable vaccine(s), the vaccine(s) should be administered at different injection sites.

Do not mix FLUAD QUADRIVALENT with any other vaccine in the same syringe.

Concurrent Use With Immunosuppressive Therapies: Immunosuppressive or corticosteroid therapies may reduce the immune response to FLUAD QUADRIVALENT.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

FLUAD QUADRIVALENT is not approved for use in persons < 65 years of age. There are insufficient human data to establish whether there is a vaccine-associated risk with use of FLUAD QUADRIVALENT in pregnancy.

There were no developmental toxicity studies of FLUAD QUADRIVALENT performed in animals. A developmental toxicity study has been performed in female rabbits administered FLUAD (trivalent formulation) prior to mating and during gestation. A 0.5 mL dose was injected on each occasion (a single human dose is 0.5 mL).

Lactation

Risk Summary

FLUAD QUADRIVALENT is not approved for use in persons < 65 years of age.
No human or animal data are available to assess the effects of FLUAD QUADRIVALENT on the breastfed infant or on milk production/excretion.

Pediatric Use

Safety and effectiveness of FLUAD and FLUAD QUADRIVALENT (same manufacturing process and overlapping composition with FLUAD) were evaluated in clinical trials conducted in children 6 months to <72 months of age. Data from these trials are inconclusive to demonstrate the safety and effectiveness of FLUAD QUADRIVALENT in children 6 months to <72 months of age. The safety and effectiveness of FLUAD QUADRIVALENT in infants less than 6 months of age and in children older than 72 months of age have not been evaluated.

Geriatric Use

Safety and immunogenicity of FLUAD QUADRIVALENT have been evaluated in adults 65 years of age and older.

REFERENCE

1. Lasky T, Terracciano GJ, Magder L, et al. The Guillain-Barré syndrome and the 1992-1993 and 1993-1994 influenza vaccines. *N Engl J Med* 1998; 339(25):1797-1802.

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

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