FLUAD™ (Influenza Vaccine, Adjuvanted) for Patients Aged 65 Years and Older:

Safety Overview

INDICATIONS AND USAGE[1]

FLUAD is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUAD is approved for use in persons 65 years of age and older. Approval is based on the immune response elicited by FLUAD. Data demonstrating a decrease in influenza disease after vaccination with FLUAD are not available.

CONTRAINDICATIONS[1]

Do not administer FLUAD 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 accompanying US full Prescribing Information for FLUAD.

FLUAD™
influenza vaccine, adjuvanted

FLUAD (Influenza Vaccine, Adjuvanted) Safety Profile

Clinical Trials Experience[1]

- In the pivotal phase 3 study, the most common (≥10%) solicited local adverse reactions in elderly adults (≥65 years of age) were injection site pain (25%) and tenderness (21%).
- The most common solicited systemic adverse reactions observed were myalgia (15%), headache (13%), and fatigue (13%).
- While higher rates of solicited adverse reactions were noted, they were typically mild to moderate in severity.

FLUAD: Solicited local adverse reactions[1]

		FLUAD N[b] = 3418-3496 %	AGRIFLU[a] N[b] = 3420-3488 %
Injection site pain	Any	25.0	12.2
	Moderate[c]	3.9	1.9
	Severe[d]	0.3	0.2
Tenderness	Any	21.1	11.2
	Moderate	3.0	1.0
	Severe	0.1	0.2
Erythema	Any	1.2	0.5
	25 to ≤50 mm	1.1	0.5
	51 to ≤100 mm	0.2	<0.1
	>100 mm	0.0	0.0
Induration	Any	1.3	0.5
	25 to ≤50 mm	1.0	0.5
	51 to ≤100 mm	0.3	0.0
	>100 mm	0.0	0.0
Swelling	Any	1.2	0.4
	25 to ≤50 mm	1.0	0.4
	51 to ≤100 mm	0.2	<0.1
	>100 mm	<0.1	0.0

[a]AGRIFLU (influenza vaccine) is a US-licensed nonadjuvanted influenza vaccine.

[b]N = number of subjects with safety data.

[c]Moderate: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "some limitation in normal daily activity," diarrhea defined as "4 to 5 stools a day."

[d]Severe: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "unable to perform normal daily activity," diarrhea defined as "6 or more watery stools a day."

FLUAD: Solicited systemic adverse reactions[1]:

		FLUAD N[b] = 3418-3496 %	AGRIFLU[a] N[b] = 3420-3488 %
Myalgia	Any	14.7	9.7
	Moderate[c]	2.6	1.8
	Severe[d]	0.3	0.7
Fatigue	Any	13.3	10.4
	Moderate	3.1	2.4
	Severe	0.4	0.6
	PLT[e]	0.0	<0.1
Headache	Any	13.2	11.2
	Moderate	3.0	2.6
	Severe	0.4	0.6
	PLT	0.0	<0.1
Arthralgia	Any	8.5	7.8
	Moderate	1.6	1.6
	Severe	0.2	0.6
Chills	Any	6.7	4.7
	Moderate	1.5	1.2
	Severe	0.3	0.3
	PLT	<0.1	0.0
Diarrhea	Any	4.8	4.5
	Moderate	1.3	0.9
	Severe	0.3	0.2
	PLT	<0.1	<0.1
Fever	Any	3.6	3.4
	≥38.0°C to ≤38.4°C	1.8	1.7
	≥38.5°C to ≤38.9°C	1.3	1.3
	39.0°C to ≤40.0°C	0.4	0.4
	≥40.0°C	0.1	0.0
Nausea	Any	2.9	2.8
	Moderate	0.4	0.6
	Severe	0.1	0.1
	PLT	<0.1	0.0
Vomiting	Any	1.4	1.7
	Moderate	0.4	0.5
	Severe	<0.1	0.1
	PLT	<0.1	0.0

[a]AGRIFLU (influenza vaccine) is a US-licensed nonadjuvanted influenza vaccine.

[b]N = number of subjects with safety data.

[c]Moderate: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "some limitation in normal daily activity," diarrhea defined as "4 to 5 stools a day."

[d]Severe: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "unable to perform normal daily activity," diarrhea defined as "6 or more watery stools a day."

[e]Potentially life threatening (PLT) reaction defined as requiring emergency room visit or hospitalization.

Pooled Safety Data From 15 Randomized Clinical Trials

Unsolicited Adverse Events and Adverse Events of Special Interest[1]

- The clinical safety of FLUAD was assessed in 15 randomized controlled studies.
- The total safety population in these trials included 10,952 adults 65 years and older, 5754 who received FLUAD and 5198 who received other US-licensed influenza vaccines.
- The percentage of subjects with an unsolicited adverse event (AE) within 30 days following vaccination was similar between vaccine groups.
- Rates of new onset neuroinflammatory and immune-mediated diseases were assessed in a post hoc analysis of the 15 randomized controlled studies over 1 year. The percentage of subjects with an adverse event of special interest (AESI) at any time after vaccination was also similar between vaccine groups. There were no notable imbalances for specific AESIs.

Unsolicited AEs and AESIs in 15 randomized controlled trials[1]

	FLUAD N = 5754 %	Comparator[a] N = 5198 %
Unsolicited AE	16.9	18.0
AESI	0.9	0.9

[a] Other US-licensed influenza vaccines.

Serious Adverse Events and Deaths[1]

- Subjects in Study 1 were followed for 1 year following vaccination.
- The percentage of subjects with an SAE was similar between vaccine groups.
  - Four SAEs (1 FLUAD and 3 AGRIFLU) were considered to be related to study vaccination over 1 year of observation; 2 of these occurred (1 FLUAD, 1 AGRIFLU) within 21 days of vaccination.
- In the 1-year postvaccination, there were 98 deaths (n = 52 FLUAD, n = 46 AGRIFLU); none occurred within 21 days of vaccination.

SAEs and deaths in study 1[1]

	FLUAD N = 3545	AGRIFLU N = 3537
SAE, %	7	7
Deaths, n	52	46

- The number of SAEs and deaths was also monitored in 14 additional randomized controlled studies.
  - The percentages of SAEs and deaths within 30 days and within 6 months were similar between vaccine groups.

SAEs and deaths in 14 randomized controlled studies[1]

	FLUAD N = 2209	Comparator[a] N = 1661
Percentage of subjects with SAEs		
Within 30 days	1.1	1.8
Within 6 months	4.3	5.9
Percentage of deaths		
Within 30 days	0.3	0.6
Within 6 months	1.0	1.5

[a] The comparator for SAEs was AGRIFLU; the comparator for deaths was other US-licensed vaccines.

Safety of Annual Revaccination[1]:

- In 5 of the randomized controlled trials, subjects were followed for SAEs and deaths for 6 months following revaccination.
  - The percentage of subjects with an SAE reported after the second annual revaccination was similar between groups.
  - None of the 23 reported deaths were considered to be related to study vaccination.

SAEs and deaths reported after second annual vaccination with FLUAD or comparator influenza vaccines[1]:

	FLUAD N = 492	Comparator[a] N = 330
SAE, %	6.1	5.5
Deaths, n	17	6

[a] US-licensed and non-US-licensed influenza vaccines.

Safety population in 15 additional clinical trials:

10,952 adults

65 years and older

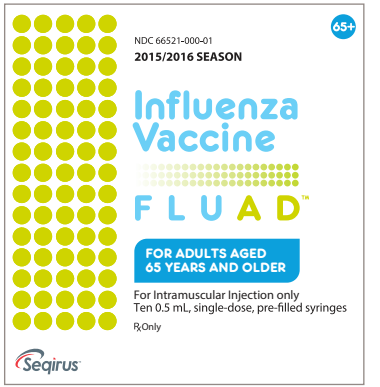
- 5754 received FLUAD
- 5198 received other US-licensed influenza vaccines

Dosage and Administration of FLUAD[1]

For intramuscular injection only.

- Administer FLUAD as a single 0.5 mL intramuscular injection in adults 65 years of age and older.
- Gently shake each syringe. FLUAD has a milky white appearance. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit.
  - If either condition exists, FLUAD should not be administered.
- The vaccine should be administered by intramuscular injection, preferably in the region of the deltoid muscle of the upper arm.
  - Do not inject the vaccine in the gluteal region or areas where there may be a major nerve trunk.
- FLUAD does not contain latex. Please note: the tip caps of the prefilled syringes contain latex.
- FLUAD does not contain a preservative.

CPT Code: 90653



References: 1. FLUAD [package insert]. Holly Springs, NC: Seqirus, Inc; 2015. **2.** O'Hagan D, Ott G, De Gregorio E, Seubert A. The mechanism of action of MF59 - an innately attractive adjuvant formulation. *Vaccine*. 2012;30:4341-4348. doi:10.1016/j.vaccine.2011.09.06.

Introducing FLUAD (Influenza Vaccine, Adjuvanted)

Indication[1]

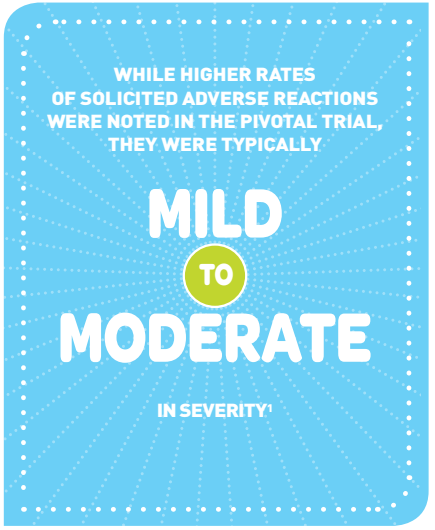
FLUAD is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUAD is approved for use in persons 65 years of age and older. Approval is based on the immune response elicited by FLUAD. Data demonstrating a decrease in influenza disease after vaccination with FLUAD are not available.

Contraindications[1]

Do not administer FLUAD 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.

Additional Information on FLUAD[1,2]

- FLUAD is a trivalent inactivated influenza vaccine.
- Each 0.5 mL dose contains at least 15 mcg of hemagglutinin of each influenza strain recommended for the current influenza season and the MF59® oil-in-water emulsion as adjuvant.
  - Studies in animals and humans suggest that MF59 recruits immune cells to the site of injection and enhances their activity.
- FLUAD does not contain a preservative.
- The tip caps of the prefilled syringes contain natural rubber latex. The syringe and syringe plunger stopper are not made with latex.



Important Safety Information[1]

Indications and Usage

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

Contraindications

Severe allergic reaction to any component of the vaccine, including egg protein, or after a previous dose of any influenza vaccine.

Warnings and Precautions

- If Guillain-Barré Syndrome (GBS) has occurred within six weeks of previous influenza vaccination, the decision to give FLUAD should be based on careful consideration of the potential benefits and risks.
- The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions in latex sensitive individuals.

Adverse Reactions

- The most common (≥10%) local (injection-site) adverse reactions observed in clinical studies were injection site pain (25%) and tenderness (21%).
- The most common (≥10%) systemic adverse reactions observed in clinical studies were myalgia (15%), headache (13%) and fatigue (13%).

Please see accompanying US full Prescribing Information for FLUAD.

Notes:

Visit www.**FLUAD.com** for more information.

Seqirus™

Seqirus Inc.
Holly Springs, North Carolina 27540

January 2016

GMCC-697_2016-1-13_S

FLUAD™
influenza vaccine, adjuvanted