PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

FLUAD® Pediatric and FLUAD®

(Influenza Vaccine, Surface Antigen, Inactivated, Adjuvanted with MF59C.1)

Sterile Suspension for Intramuscular Injection

Active Immunizing Agent for the Prevention of Influenza

ATC: J07BB02

2025 – 2026 Strains:

A/Victoria/4897/2022 IVR-238 (an A/Victoria/4897/2022 (H1N1) pdm09-like virus),

A/Croatia/10136RV/2023 X-425A (an A/Croatia/10136RV/2023 (H3N2)-like virus),

B/Austria/1359417/2021 BVR-26 (a B/Austria/1359417/2021-like virus)

Sponsor:

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Distributed by:

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RECENT MAJOR LABEL CHANGES

Not applicable.

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

FLUAD® Pediatric/FLUAD® is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and B contained in the vaccine in the pediatric population (6 months to less than 2 years of age) and in elderly 65 years of age and older [see 14 CLINICAL TRIALS]

1.1 Pediatrics

Pediatrics (6 months to < 2 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of FLUAD® Pediatric in pediatric population has been established. Therefore, Health Canada has authorized an indication for use in this pediatric age group. It is administered as a 0.25 ml injection.

Pediatrics (2- <18 years of age): The safety and efficacy of FLUAD® Pediatrics in children from 2 years to less than 18 years has not been established. Therefore, Health Canada has not authorized an indication for use in this pediatric age group.

1.2 Geriatrics

Geriatrics: Based on the data submitted and reviewed by Health Canada, the safety and efficacy of FLUAD® in adult patients 65 years of age and older has been established; therefore, Health Canada has authorized an indication for geriatric use. It is administered as a 0.5 ml injection.

2 CONTRAINDICATIONS

FLUAD® Pediatric/FLUAD® is contraindicated in persons with a known hypersensitivity to the active substances, to any of the excipients and to eggs, chicken proteins, kanamycin and neomycin sulphate, hydrocortisone, formaldehyde, and cetyltrimethylammonium bromide (CTAB), or in anyone who has had a life-threatening reaction to previous influenza vaccination.

For a complete listing of ingredients in the formulation and components of the container, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

4.1 Dosing Considerations

Administration with Other Vaccines

FLUAD® Pediatric/FLUAD® should not be mixed with other vaccines in the same syringe. Separate injection limbs should be used if more than one vaccine is being administered during the same visit. (See 9.4 Drug-Drug Interactions)

4.2 Recommended Dose

Pediatric population (children 6 months to less than 2 years of age)

Table 1 – Recommended Dose for Pediatric population

	Pediatric subjects who are being vaccinated for the first time against seasonal influenza or Pediatric Subjects who were vaccinated for the first time last season with only *one* dose of influenza vaccine	Pediatric subjects who have been previously vaccinated with two doses of any seasonal influenza vaccine in a previous season
Infants and children from 6 months to less than 2 years:	Two 0.25 mL doses 4 weeks apart	One 0.25 mL dose

When FLUAD® Pediatric is to be given as two doses, it is recommended that the same vaccine and dose is given for both vaccinations. There are no data to support the use of FLUAD® Pediatric as the first dose, and another influenza vaccine as the second dose. If FLUAD® Pediatric is not available at the time of the second dose, the clinician should use best judgment to complete the vaccination.

As is with other influenza vaccines, children who have received the appropriate course of FLUAD® Pediatric or another seasonal influenza vaccine are considered to be primed. These children may receive a single age-appropriate dose of influenza vaccine prior to the next influenza season. There are limited data to study the usage of FLUAD® Pediatric in children in more than 1 influenza season. These data indicate that FLUAD® Pediatric may be given to children in more than 1 influenza season.

Elderly population (Adults 65 years of age and older)

A single 0.5 mL dose administered once a year.

FLUAD® should under no circumstances be administered by any other route than intramuscularly.

4.4 Administration

Gently shake the contents of each syringe to aid inspection for the presence of particulate matter. After

shaking, the normal appearance of FLUAD® Pediatric/FLUAD® is a milky-white suspension.

If there are visible particles, allow the vaccine to come to room temperature and shake before use (FLUAD® Pediatric/FLUAD® can be kept at room temperature (20º-25ºC) for up to 2 hours as a holding time before injection).

Do not use the vaccine if particles remain, if it is discoloured, or if it has been frozen.

Before immunization, the skin over the site to be injected should be cleansed with a suitable germicide.

FLUAD® Pediatric/FLUAD® should be administered as a single intramuscular injection preferably in the region of the deltoid muscle of the upper arm. The vaccine should not be injected in the gluteal region or areas where there may be a major nerve trunk.

FLUAD® Pediatric/FLUAD® should under no circumstances be administered by any other route than intramuscularly.

5 OVERDOSAGE

There is no experience of overdose with FLUAD® Pediatric/FLUAD®.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength	Non-medicinal Ingredients
Intramuscular injection	Parenteral / Each 0.25 mL dose contains 7.5 mcg of influenza virus haemagglutinin surface antigens from each of the three virus strains, types A and B (see 13 PHARMACEUTICAL INFORMATION)	Polysorbate 80 *For a complete listing see Composition.*
	Parenteral / Each 0.5 mL dose contains 15 mcg of influenza virus haemagglutinin surface antigens from each of the three virus strains, types A and B (see 13 PHARMACEUTICAL INFORMATION)	

Dosage Forms

FLUAD® Pediatric is a sterile milky-white suspension for intramuscular injection in 1 mL prefilled syringes containing a 0.25 mL dose.

FLUAD® is a sterile milky-white suspension for intramuscular injection in 1 mL prefilled syringes containing a 0.5 mL dose.

Composition

- Active Ingredients:

− influenza virus haemagglutinin (HA) and neuraminidase (NA) from each of the following 3 strains recommended by the World Health Organization (WHO) for the 2025/2026 season:

	0.25 mL dose	*0.5 mL dose*
A/Victoria/4897/2022 (H1N1)pdm09-like virus	7.5 mcg (HA)	15 mcg (HA)
A/Croatia/10136RV/2023 (H3N2)-like virus	7.5 mcg (HA)	15 mcg (HA)
B/Austria/1359417/2021-like virus	7.5 mcg (HA)	15 mcg (HA)

- Other Ingredients:

− *Adjuvant:* MF59C.1	*0.25 mL dose*	*0.5 mL dose*
citric acid	0.02 mg	0.04 mg
polysorbate 80	0.5875 mg	1.175 mg
sodium citrate	0.33 mg	0.66 mg
sorbitan trioleate	0.5875 mg	1.175 mg
Squalene	4.875 mg	9.75 mg
water for injection		

− *Excipients:*		
calcium chloride dehydrate	0.03 mg	0.06 mg
disodium phosphate dehydrate	0.335 mg	0.67 mg
magnesium chloride hexahydrate	0.025 mg	0.05 mg
potassium chloride	0.05 mg	0.10 mg
potassium dihydrogen phosphate	0.05 mg	0.10 mg
sodium chloride	2.00 mg	4.00 mg
water for injection	to volume	to volume

− *Manufacturing Process Residuals:*

The vaccine may contain trace amounts of the following:
cetyltrimethylammonium bromide (CTAB) (residual)
formaldehyde (residual)
hydrocortisone (trace)
kanamycin (trace)
neomycin (trace)
ovalbumin (egg protein, residual)

The syringe plunger does not contain latex and FLUAD® Pediatric/FLUAD® is considered safe for use in persons with latex allergies.

Packaging

FLUAD® Pediatric/FLUAD® is supplied in packages containing one or ten single dose prefilled glass syringes (Type I), without needles.

Not all pack sizes may be marketed.

7 WARNINGS AND PRECAUTIONS

General

FLUAD® Pediatric/FLUAD® should under no circumstances be administered by any other route than intramuscularly.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Prior to administration of any dose of FLUAD® Pediatric/FLUAD®, the vaccine recipient should be asked about personal medical history, family medical history, recent and current health status, including immunization history, main allergies and any adverse events associated with previous immunizations.

Before the injection of any biological product, such as vaccines, the person responsible for administration should take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration of the vaccine.

Immunization with FLUAD® Pediatric/FLUAD® should be postponed in patients with febrile illness or acute infections.

Hematologic

As with other intramuscular injections, administration of FLUAD® Pediatric/FLUAD® requires careful consideration in patients with clinically significant bleeding disorders.

Immune

The immune response to FLUAD® Pediatric/FLUAD® in immunocompromised persons, including individuals receiving immunosuppressive therapy, may be lower than in immunocompetent individuals. Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Monitoring and Laboratory Tests

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, hepatitis C and, especially HTLV1 have been observed. The Western Blot technique disproves the results. The transient false positive reactions could be due to the IgM response by the vaccine.

Neurologic

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUAD® Pediatric/FLUAD® should be based on careful consideration of the potential benefits and risks.

Skin

See 8 ADVERSE REACTIONS, Clinical Trial Adverse Reactions and Post-Market Adverse Reactions.

7.1 Special Populations

7.1.1 Pregnant Women

FLUAD® Pediatric/FLUAD® is indicated for use in the pediatric population of 6 months to less than 2 years of age and adults 65 years of age and older, respectively; there is no pregnancy information applicable to these populations.

7.1.2 Breast-feeding

No human or animal data are available to assess the effects of FLUAD® Pediatric/FLUAD® on the breastfed infant or on milk production/excretion.

7.1.3 Pediatrics

See 1 INDICATIONS, Pediatrics.

7.1.4 Geriatrics

See 1 INDICATIONS, Geriatrics.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Adverse event information is derived from both controlled and uncontrolled clinical trials and worldwide post-marketing experience.

Vaccination with FLUAD® Pediatric/FLUAD® cannot cause influenza because the vaccine does not contain live virus. Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination.

Allergic-type responses, such as urticarial rash, allergic bronchospasm, or systemic anaphylaxis uncommonly or rarely occurred in clinical trials. Anaphylactic shock has been reported in rare post-marketing cases.

The most common local adverse drug reactions in the pediatric population are erythema and tenderness. The incidence of pediatric subjects reporting any solicited systemic reactions was generally slightly higher in the FLUAD® Pediatric group than in the comparator group (42% vs. 38%).

The most common FLUAD® local adverse drug reactions in the elderly are pain at the injection site, temperature at the injection site, and erythema. The incidence of elderly subjects reporting any solicited systemic reactions was generally slightly higher in the FLUAD® group than in the comparator group (17% vs. 12%). Reactions are generally mild or moderate and of limited duration. Prophylactic acetaminophen may decrease the frequency of some side effects in adults.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Adults 65 Years of Age and Older

The safety profile of FLUAD® in adults 65 years and older is based on data from 39 studies. Overall 12,889 subjects were exposed to at least one dose with FLUAD®. Of these 492 received a second consecutive vaccination one year later, and 150 a third FLUAD® vaccine dose the following year. In one study, two doses of FLUAD® were administered 4 weeks apart. In 38 studies solicited local (injection

site) and systemic reactions were collected from subjects who completed a symptom diary card for at least four days following vaccination.

Safety data after first vaccination for subjects 65 years of age and older were pooled from 31 trials, safety data after second consecutive vaccination were pooled from five studies and after third consecutive vaccination from two studies.

Pooled Reactogenicity data are provided in Table 3, Table 4 and Table 5.

The most frequently reported solicited local adverse events within 4 days of vaccination were injection site pain, followed by temperature at the injection site ("warm" or "hot") and erythema. Local injection-site reactions (pain and temperature at the injection site) were more frequent in subjects who received the MF59 adjuvanted vaccine than in those who received nonadjuvanted vaccine. The frequency of pain was 26% in the FLUAD® group vs. 14% in the comparator group. Temperature at the injection site was 18% in the FLUAD® group vs 11% in the comparator group. Solicited local reactions were generally of mild or moderate intensity, and generally resolved within 2-3 days with 3% or less of subjects reporting a severe local reaction.

The most frequently reported solicited systemic adverse events were headache, fatigue, malaise and myalgia. Most reports of systemic reactions were mild to moderate in severity and generally transient, with 1% or less of subjects reporting a severe systemic reaction across all studies.

In the subset of subjects who received second and third consecutive vaccinations, for both the FLUAD® and the comparator vaccines groups, there was a trend for an increase in the percentage of subjects reporting each local reaction during the 3 days after the second vaccination, compared to the first vaccination, but no further increase after the third vaccination. Overall, systemic reactions were reported by similar percentages of subjects after the first, second, and third vaccinations in both the FLUAD® and comparator vaccines groups.

Table 3 – Any (Severe[a]) Local and Systemic Reactions in Elderly Subjects ≥65 Years (Days 0-3) After One Vaccination - Pooled Studies

Reaction	Percentages of Subjects with Any (Severe[a]) Solicited Reaction	
	FLUAD®	**Comparator**
	N = 3713	**N = 1656**
Subjects with Any Solicited Local Reaction	**37**%	**30**%
Pain at injection site	26% (<1%) *N = 3712*	14% (<1%)
Temperature at injection site	18% (1%) *N = 2265*	11% (1%) *N = 1438*
Ecchymosis	3% (<1%) *N = 1272*	2% (0) N = 44
Induration	11% (1%) *N = 3712*	9% (1%) *N = 1655*
Erythema	14% (1%) *N = 3712*	14% (1%) *N = 1655*
Swelling	5% (1%) *N = 1447*	6% (1%) *N = 218*
Subjects with Any Solicited Systemic Reaction	**17%**	**12%**
Chills	3% (<1%) *N = 3712*	2% (<1%) *N = 1655*
Fatigue	6% (<1%) *N = 1493*	7% (1%) *N = 264*
Headache	6% (<1%) *N = 3712*	5% (1%) *N = 1655*
Malaise	6% (<1%) *N = 3712*	5% (<1%) *N = 1655*
Myalgia	7% (<1%) *N = 3712*	3% (<1%) *N = 1655*
Nausea	2% (<1%) *N = 2581*	2% (<1%) *N = 1655*
Rash	<1% (<1%) *N = 2230*	<1% (<1%) *N = 1365*
Sweating	3% (0) *N = 1447*	3% (<1%) *N = 218*
Arthralgia	4% (<1%) *N = 3666*	2% (<1%) *N = 1609*
Fever (≥38°C/≥40°C)	1% (0) *N = 3675*	<1% (0) *N = 1652*

[a] Defined as ecchymosis, erythema, induration, and swelling >50mm; temperature at injection site "hot"; rash "urticaria"

Table 4 – Any (Severe[a]) Local and Systemic Reactions in Elderly Subjects ≥65 Years (Days 0-3) Who Received Two Consecutive FLUAD® Vaccinations One Year Apart, by Vaccination

	Percentages of Subjects with Any (Severe[a]) Solicited Reaction			
	1st Vaccination		2nd Vaccination	
	FLUAD® N=487	Comparator N=329	FLUAD® N=487	Comparator N=329
Solicited Local Reactions				
Pain at injection site	19% (1%)	7% (0)	27% (1%)	21% (<1%)
Temperature at injection site	6% (2%)	4% (1%)	15% (3%)	12% (2%)
Induration	9% (1%)	6% (1%)	13% (1%)	10% (<1%)
Erythema	9% (1%)	6% (0)	23% (2%)	20% (3%)
Solicited Systemic Reactions				
Chills	4% (<1%)	4% (<1%)	3% (0)	2% (0)
Fatigue	15% (0) *N=39*	0 *N=35*	0 *N=39*	3% (0) *N=35*
Headache	5% (<1%)	5% (<1%)	8% (0)	5% (0)
Malaise	7% (<1%)	6% (0)	8% (0)	6% (<1%)
Myalgia	4% (<1%)	2% (<1%)	3% (0)	2% (0)
Nausea	3% (0)	2% (0)	2% (0)	3% (<1%)
Rash	<1% (<1%) *N=306*	<1% (0) *N=222*	<1% (<1%)	<1% (0)
Arthralgia	2% (<1%) *N=448*	1% (<1%) *N=294*	1% (0)	2% (0)
Fever (≥38°C/≥40°C)	1% (0)	0	1% (0)	1% (0)

[a]Severe defined as: induration, erythema and swelling >50mm; temperature at injection site "hot"; rash "urticaria"

Table 5 – Any (Severe[a]) Solicited Local and Systemic Reaction in Elderly Subjects ≥65 Years (Days 0-3) Who Received Three Consecutive FLUAD® Vaccinations One Year Apart, by Vaccination

Reaction	Percentages of Subjects with Any (Severe[a]) Solicited Reaction					
	1st Vaccination		2nd Vaccination		3rd Vaccination	
	FLUAD® N=149	Comp. N=87	FLUAD® N=150	Comp. N=87	FLUAD® N=150	Comp. N=87
Solicited Local Reactions						
Pain at injection site	28% (1%)	5% (0)	29% (1%)	15% (0)	28% (1%)	16% (0)
Temperature at injection site	4% (1%)	5% (0)	7% (1%)	2% (1%)	12% (1%)	7% (0)
Induration	8% (0)	5% (0)	12% (1%)	6% (0)	13% (1%)	6% (0)
Erythema	9% (0)	6% (0)	14% (1%)	7% (1%)	22% (3%)	9% (0)
Solicited Systemic Reactions						
Chills	4% (0)	6% (1%)	1% (0)	2% (0)	3% (0)	0
Fatigue	17% (0)	0	0 *(N=35)*	3%*(N=32)*	- *(N=0)*	- *(N=0)*
Headache	4% (0)	2% (0)	8% (0)	5% (0)	4% (1%)	3% (0)
Malaise	7% (0)	3% (0)	5% (0)	3% (0)	7% (0)	3% (0)
Myalgia	3% (0)	1% (1%)	5% (0)	2% (0)	1% (0)	2% (0)
Nausea	2% (0)	0	3% (0)	2% (0)	3% (0)	2% (0)
Rash	- *(N=0)*	- *(N=0)*	0 *(N=115)*	0 *(N=55)*	0	0
Arthralgia	2% (0)	2% (2%)	1% (0)	3% (0)	1% (0)	3% (0)
Fever (≥38°C)	0	0	1% (0)	0	1% (0)	0

[a]Severe defined as: induration, erythema and swelling >50mm; temperature at injection site "hot"; rash "urticaria"; Comp.= comparator vaccine

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Children 6 months to less than 2 years of age

The safety of FLUAD® Pediatric was assessed in six randomized clinical trials that involved 4091 infants and children 6 months to less than 2 years of age (FLUAD® Pediatric: 1800; conventional non-adjuvanted trivalent and investigational quadrivalent influenza comparator vaccines: 2083; other non-influenza control vaccines: 208).

The most frequently reported solicited local reaction after each vaccination was erythema, followed by tenderness. Most local reactions were mild or moderate, and 1% or fewer subjects experienced severe reactions.

The most frequently reported solicited systemic reaction after each vaccination was irritability, followed by sleepiness and body temperature ≥38°C. Most systemic reactions were mild or moderate, and <1% of subjects experienced severe reactions. After the first vaccination with FLUAD® Pediatric, 17% of subjects experienced fever (body temperature ≥38°C) compared with 12% to 16% after the first vaccination with the non-adjuvanted influenza comparator.

Pooled reactogenicity data are provided in Table 6.

Table 6 – Any Solicited Reactions After First and Second Vaccinations in Children 6 Months to <2 Years of Age

	Percentages of Subjects with Any[a] Solicited Reaction[b]					
	After First Vaccination			After Second Vaccination		
	FLUAD® Pediatric	Comp. 1	Comp. 2	FLUAD® Pediatric	Comp. 1	Comp. 2
	N=1799	N=1457	N=622	N=1704	N=1379	N=606
Solicited Local Reactions						
Erythema	19%	17%	13%	21%	17%	11%
Tenderness	13%	11%	5%	11%	9%	4%
Induration	7%	5%	3%	9%	5%	2%
Ecchymosis	5%	5%	4%	5%	5%	2%
Swelling	3%	3%	1%	4%	3%	<1%
Solicited Systemic Reactions[c]						
Irritability	23%	22%	16%	18%	17%	9%
Body Temp. (≥ 38C)	17% N=1798	16%	12%	19%	16%	13%
Sleepiness	19%	16%	14%	14%	12%	6%
Change in eating habits	15%	16%	12%	12%	10%	6%
Diarrhea	15%	15%	14%	12%	9%	12%
Persistent crying	11% N=829	11% N=560	10% N=557	7% N=809	6% N=539	5% N=545
Vomiting	7%	7%	5%	5%	4%	5%

[a] Severe reactions were reported in zero to less than 1% of subjects

[b] N represents the total number of subjects exposed during the observation period (30 minutes to 7 days) post-vaccination

[c] After first vaccination: FLUAD® Pediatric N = 1800, Comp. 1 N= 1458, and Comp. 2 N = 622. After second vaccination: FLUAD® Pediatric N = 1704, Comp. 1 N= 1379, and Comp. 2 N = 606

Comp. = Comparator; Comp. 1 = Agrippal, Influsplit, Fluzone and Vaxigrip; Comp. 2 = AGRIFLU® and Quadrivalent vaccine comparator

During clinical trials of FLUAD® Pediatric, rhinitis, cough, upper respiratory tract inflammation, and nasopharyngitis were reported as temporally related unsolicited adverse events in both pediatric age groups. In addition, the following unsolicited adverse events of note were reported within 3 weeks of vaccination as at least possibly related: 1 case of febrile convulsion, 13 cases of rash, and 1 case of anaphylactic reaction.

8.3 Less Common Clinical Trial Adverse Reactions

See 8 ADVERSE REACTIONS, Clinical Trial Adverse Reactions.

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

See 8 ADVERSE REACTIONS, Clinical Trial Adverse Reactions - Pediatrics.

8.5 Post-Market Adverse Reactions

Because post-marketing reporting is voluntary in a population of uncertain size, it is not possible to estimate the frequency of an adverse event and is also often difficult to establish its causal relationship to vaccine exposure.

The adverse events described below have been included because: a) they represent reactions that are known to occur following immunizations generally or influenza immunizations specifically; b) they are potentially serious; or c) of the frequency of reporting. The following additional adverse reactions have been the subject of spontaneous reports during post-approval use of FLUAD® since 2003.

General disorders and administration site conditions:

Local injection site reactions including redness, swelling, pain at the injection site, ecchymosis, induration. Extensive swelling of injected limb, injection-site cellulitis-like reaction, peripheral swelling, asthenia

Immune system disorders:

Allergic reactions including anaphylaxis and rarely reported anaphylactic shock.

Vascular disorders:

Vasculitis (in rarely reported cases associated with transient renal involvement).

Blood and lymphatic system disorders:

Thrombocytopenia (including rarely reported severe cases with platelet counts less than 5,000 per mm^3), lymphadenopathy.

Musculoskeletal and connective tissue disorders:

Muscular weakness, pain in extremity

Nervous system disorders:

Neuralgia, paraesthesia, convulsion, myelitis (including encephalomyelitis and transverse myelitis), neuritis, Guillain-Barré Syndrome, dizziness, syncope, presyncope.

Skin and subcutaneous tissue disorders:

Generalized skin reactions including exudative erythema multiforme, pruritus, urticaria, non-specific rash, angioedema.

There is limited post-marketing experience with FLUAD® Pediatric in infants and children.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No interaction between FLUAD® Pediatric/FLUAD® and other vaccines or medication are known.

9.4 Drug-Drug Interactions

FLUAD® may be given at the same time as other vaccines. There are no data to assess the concomitant administration of FLUAD® Pediatric with other vaccines. FLUAD® Pediatric/FLUAD® should not be mixed with any other vaccine in the same syringe. Immunization should be carried out on separate limbs. It should be noted that any adverse reactions may be intensified.

Although a possible interaction has been suggested in the literature between influenza vaccination and the use of warfarin and theophylline, clinical studies have not shown any adverse effects attributable to these drugs in people receiving influenza vaccine. There were no studies designed to evaluate the drug interactions with FLUAD® Pediatric/FLUAD®.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Influenza illness and its complications follow infection with influenza viruses. Global surveillance of influenza identifies yearly antigenic variants. For example, since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation. Specific levels of hemagglutination inhibition (HI) antibody titers induced by vaccination with inactivated influenza virus vaccine have not been correlated with protection from influenza illness. Some studies of influenza infection, including human challenge studies following vaccination, have suggested that HI antibody titers ranging from 1:15 to 1:65 may be associated with protection from illness in 50% of subjects and protection from illness is increased with higher titers.

Antibody against one influenza virus type or subtype may confer limited or no protection against another. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Frequent development of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the usual change of one or more new strains in each year's influenza vaccine. Therefore, inactivated influenza vaccines are standardized to contain the hemagglutinin of influenza virus strains (typically two type A and one type B), representing the influenza viruses likely to be circulating in Canada during the upcoming flu

season, on the basis of the recommendations from the World Health Organization (WHO) and the National Advisory Committee on Immunization (NACI).

Annual revaccination with the current vaccine is recommended because immunity declines during the year after vaccination, and because circulating strains of influenza virus change from year to year.

10.2 Pharmacodynamics

The antibody response to FLUAD® is increased when compared to the response to vaccines without adjuvant, and is most pronounced for A/H3N2 and B influenza antigens. Seroprotection is generally obtained within 2 to 3 weeks after vaccination.

Similarly, development of antibody levels associated with protection against disease is generally obtained within 2 to 3 weeks after a single dose in children who have been previously vaccinated against influenza. Children who have not been previously vaccinated against influenza develop protective antibody responses within 2 to 3 weeks after the second vaccine dose.

This increased response is seen particularly in elderly subjects with low pre-immunization titre and/or with underlying diseases (diabetes, cardiovascular and respiratory diseases) who are at increased risk of complications of influenza infection. A similar immunogenicity profile has been noted after a second and third immunization with FLUAD®.

Consistent higher antibody titers after immunization with FLUAD® Pediatric/FLUAD® have also been observed against homologous and heterologous strains. The difference in antibody responses with FLUAD® administered in the elderly population was statistically significant for some strains and/or some endpoints compared with the comparator.

10.3 Pharmacokinetics

Not applicable.

Duration of Effect

The duration of post-vaccination immunity to homologous strains or to strains closely related to the vaccine strains varies, but it is usually 6-12 months.

Special Populations and Conditions

Not applicable.

11 STORAGE, STABILITY AND DISPOSAL

Store FLUAD® Pediatric/FLUAD® between 2°C and 8°C. Do not freeze. Do not use if vaccine has been frozen. Protect from light. Do not use vaccine after expiration date.

FLUAD® Pediatric/FLUAD® can be administered following a 2 hour exposure at temperatures between 8° and 25°C. This is not, however, a recommendation for storage.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Purified haemagglutinin (HA) and neuraminidase (NA) surface antigens from each of the three influenza virus strains, types A and B, recommended annually for immunization by the World Health Organisation (WHO) and the National Advisory Committee on Immunization (NACI).

Chemical name: As above

Pharmaceutical standard: The vaccine is standardized according to the WHO and NACI requirements for the [2025 – 2026] influenza season.

Product Characteristics

FLUAD® Pediatric/FLUAD® is a trivalent, surface antigen, inactivated influenza vaccine adjuvanted with MF59C.1.

The influenza virus strains are individually grown in the allantoic cavity of embryonated hens' eggs inoculated with a specific type of influenza virus suspension containing kanamycin, neomycin sulphate and hydrocortisone. Each of the influenza virus strains is harvested and clarified separately by centrifugation and filtration prior to inactivation with formaldehyde. The inactivated virus is concentrated and purified by zonal centrifugation. The surface antigens, hemagglutinin and neuraminidase, are obtained from the influenza virus particle by further centrifugation in the presence of cetyltrimethylammonium bromide (CTAB), a process which removes most of the internal proteins. The CTAB is removed from the surface antigen preparation.

The MF59C.1 adjuvant contained in FLUAD® Pediatric/FLUAD® is an oil-in-water emulsion composed of squalene as the oil phase, stabilised with the surfactants polysorbate 80 and sorbitan trioleate, in citrate buffer.

FLUAD® Pediatric/FLUAD® appears as a sterile, milky-white suspension for intramuscular injection in a prefilled syringe. It has been formulated to contain at least 7.5 mcg HA/0.25 mL dose or 15 mcg HA/0.5 mL dose of each of the following three influenza strains recommended for the 2025/2026 influenza season:

A/Victoria/4897/2022 (H1N1)pdm09-like virus (A/Victoria/4897/2022 IVR-238), A/Croatia/10136RV/2023 (H3N2)-like virus (A/Croatia/10136RV/2023 X-425A), B/Austria/1359417/2021-like virus (B/Austria/1359417/2021 BVR-26), as recommended annually for immunization by the World Health Organisation (WHO) and the National Advisory Committee on Immunization (NACI).

FLUAD® Pediatric is intended for use in the pediatric population of 6 months to less than 2 years of age. It is administered as a 0.25 mL injection.

FLUAD® is intended for use in the elderly population of 65 years of age and older and is administered as a 0.5 mL injection.

See 4 DOSAGE AND ADMINISTRATION for further information.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Pediatric Population

The immunogenicity of FLUAD® Pediatric was assessed in a randomized, controlled, observer-blinded, multicenter trial in which 6100 subjects were randomly assigned to receive two doses (4 weeks apart) of FLUAD® Pediatric (3136 subjects) or TIV 1 (Sanofi licensed split vaccine; 1478 subjects) or TIV 2 (Novartis licensed subunit vaccine; 1485 subjects).

Elderly Population

Five randomized, comparator controlled, observer blind clinical studies, were selected as pivotal studies to support the immunogenicity of FLUAD®, compared with conventional non adjuvanted influenza vaccines. Additionally, immunogenicity results of one study have been presented to support the cross reactivity to heterologous influenza strains conferred by FLUAD®. Immune responses, specifically HI antibody titers to each virus strain in the vaccine, were evaluated in sera obtained 28 days after administration of the single dose of FLUAD®.

In the five pivotal studies and the one study investigating heterologous immune response, 212, 204, 154, 150, 448, and 46 subjects 65 years and older were enrolled to receive FLUAD®.

The demographic and baseline characteristics were well balanced both between vaccine groups in each study as well as across studies. In these studies the mean age ranged from 72 to 79.1 years, sex ratio was mostly balanced except for a prevalence (72%-75%) of females in one study, and Caucasians were the most represented ethnic group across studies. As expected in a population with a high percentage of subjects with previous influenza vaccinations (63% to 97% across studies and vaccine groups), the percentage of subjects with seroprotection at baseline was relatively high.

14.2 Study Results

Pediatric Population

In the pivotal trial, antibody responses three weeks after a second dose of FLUAD® Pediatric, given to children 6 months to <6 years of age, were non-inferior to two other licensed influenza vaccines.

The antibody responses as measured by geometric mean antibody titres (GMTs) and seroconversion rates against all three homologous influenza virus antigens included in the FLUAD® Pediatric vaccine were higher than for the comparator vaccines 3 weeks after administration of the second vaccine dose (Day 50). Percentages of children with HI titres ≥40 against all three homologous influenza strains were equal to or higher for the FLUAD® Pediatric vaccine than for the comparator vaccines 3 weeks after the second dose (Table 7). The difference in antibody responses with FLUAD® administered in the elderly population was statistically significant for some strains and/or some endpoints, compared with the comparator.

Table 7 – Immunogenicity (Homologous Strains) of FLUAD® Pediatric in Children 6 months to <2 years of age at Day 50

	FLUAD® Pediatric (aTIV) N = 266	TIV 1 N = 387	TIV 2 N = 389	Ratios or differences between vaccine groups
A/H1N1				
GMR[a] (95% CI)	96 (78-118)	18 (15-21)	28 (24-34)	aTIV: TIV 1= **5.3 (4.07-6.91)** aTIV: TIV 2= **3.37 (2.59-4.39)**
% ≥40[b] (95% CI)	99.25 (97.31-99.91)	82.43 (78.26-86.09)	87.40 (83.69-90.53)	aTIV- TIV 1 = **16.82% (13.10-21.00)** aTIV- TIV 2 = **11.84% (8.60-15.60)**
% SC[c] (95% CI)	95.49 (92.25-97.65)	77.78 (73.30-81.82)	85.09 (81.16-88.48)	aTIV- TIV 1= **17.71% (12.87-22.55)** aTIV- TIV2**= 10.40% (6.07-14.73)**
A/H3N2				
GMR[a] (95% CI)	112 (93-134)	33 (29-39)	50 (43-58)	aTIV: TIV 1 = **3.35 (2.65-4.24)** aTIV: TIV 2 = **2.25 (1.78-2.84)**
% ≥40[b] (95% CI)	99.62 (97.92-99.99)	99.22 (97.75-99.84)	99.74 (98.58-99.99)	aTIV- TIV 1 = 0.40% (-1.30-1.90) aTIV- TIV 2 = -0.12% (-1.80-1.10)
% SC[c] (95% CI)	98.12 (95.67-99.39)	92.51 (89.42-94.92)	95.63 (93.09-97.43)	aTIV- TIV 1 = **5.61% (2.52-8.70)** aTIV- TIV 2= **2.49% (-0.12-5.10)**
B				
GMR[a] (95% CI)	78 (67-90)	14 (13-16)	17 (15-19)	aTIV: TIV 1 = **5.52 (4.56-6.68)** aTIV: TIV 2 = **4.72 (3.9-5.71)**
% ≥40[b] (95% CI)	98.87 (96.74-99.77)	81.40 (77.15-85.15)	87.92 (84.26-90.99)	aTIV- TIV 1 = **17.48% (13.60-21.70)** aTIV- TIV 2 = **10.95% (7.60-14.70)**
% SC[c] (95% CI)	98.12 (95.67-99.39)	79.33 (74.95-83.25)	85.35 (81.44-88.71)	aTIV- TIV 1= **18.79% (14.44-23.14)** aTIV- TIV 2 = **12.77% (8.90-16.65)**

[a]GMR = geometric mean ratio = Ratio of Day 50:Day 1 GMTs; [b]≥40 = percentage of subjects with HI titre ≥40; [c]SC = percentage of subjects with seroconversion or significant increase = the percentage of subjects achieving ≥4-fold increase in HI titre from a seropositive pre-vaccination titre (≥10), or, an HI titre ≥40 from a seronegative (<10) pre-vaccination titre. Vaccine group ratios adjusted for baseline titre. **Bold** indicates a higher antibody response in favour of the FLUAD® Pediatric group. TIV 1 = Novartis licensed subunit vaccine; TIV 2= Sanofi licensed split vaccine.

The percentage of children 6 months to <2 years of age with increasingly higher HI titres at approximately 3 weeks after the second vaccine dose were higher for FLUAD® Pediatric than for the comparator influenza vaccines (Table 8). However, the HI antibody thresholds associated with protection against influenza in children have not been established.

After six months, GMTs and percentages of children with HI titre ≥40 to homologous influenza strains remained higher for the FLUAD® Pediatric vaccine in subjects 6 months to <2 years of age than for the comparator vaccines.

Table 8 – Percentages (95% CI) of Children 6 months to <2 years of Age with HI Titres ≥40, ≥110, ≥330, ≥629 at Day 50 (approximately 3 weeks after the second vaccine dose)

	FLUAD® Pediatric (aTIV) N = 266	TIV 1 N = 387	TIV 2 N = 389	Difference between vaccine groups (aTIV – TIV 1)	Difference between vaccine groups (aTIV – TIV 2)
Titre ≥40					
A/H1N1	99.25% (97.31-99.91)	82.43% (78.26-86.09)	87.40% (83.69-90.53)	16.82% (13.10-21.00)	11.84% (8.60-15.60)
A/H3N2	99.62% (97.92-99.99)	99.22% (97.75-99.84)	99.74 % (98.58-99.99)	0.40% (-1.30-1.90)	-0.12% (-1.80-1.10)
B	98.87% (96.74-99.77)	81.40% (77.15-85.15)	87.92% (84.26-90.99)	17.48% (13.60-21.70)	10.95% (7.60-14.70)
Titre ≥110					
A/H1N1	99.25% (97.31-99.91)	72.87% (68.15-77.24)	80.21% (75.89-84.05)	26.38% (22.00-31.10)	19.04% (15.20-23.30)
A/H3N2	99.25% (97.31-99.91)	92.51% (89.42-94.92)	96.66% (94.35-98.21)	6.74% (4.10-9.90)	2.59% (0.40-4.90)
B	96.62% (93.67-98.44)	45.99% (40.95-51.10)	52.19% (47.09-57.24)	50.62% (45.10-55.80)	44.43% (39.00-49.70)
Titre ≥330					
A/H1N1	84.59% (79.68-88.71)	38.24% (33.38-43.29)	41.90% (36.95-46.98)	46.34% (39.60-52.50)	42.68% (35.90-48.90)
A/H3N2	93.23% (89.52-95.94)	52.20% (47.09-57.27)	63.75% (58.76-68.54)	41.04% (35.10-46.70)	29.48% (23.80-35.00)
B	62.78% (56.67-68.61)	20.16% (16.27-24.50)	19.02% (15.24-23.28)	42.63% (35.40-49.40)	43.76% (36.60-50.50)
Titre ≥629					
A/H1N1	78.95% (73.55 – 83.69)	35.92% (31.13 – 40.92)	38.05% (33.20 – 43.08)	43.03% (36.00-49.50)	40.90% (33.80-47.40)
A/H3N2	93.23% (89.52 – 95.94)	51.68% (46.58 – 56.76)	63.24% (58.23 – 68.04)	41.55% (35.60-47.20)	29.99% (24.30-35.50)
B	60.15% (53.99 – 66.08)	19.64% (15.80 – 23.95)	18.77% (15.01 – 23.01)	40.51% (33.30-47.30)	41.38% (34.20-48.20)

TIV1= Novartis licensed subunit vaccine; TIV 2= Sanofi licensed split vaccine

Immunogenicity Against Heterologous Strains (variants from those included in the vaccine)

The antibody responses, as measured by Geometric Mean Ratios (GMRs), against all three heterologous influenza strains were higher for FLUAD® Pediatric than those for the comparator

vaccines 3 weeks and six months after administration of the second vaccine dose (Day 50 and Day 209, respectively; Table 9 and Table 10).

Seroconversion (SC) rates against all three heterologous influenza strains were also higher for FLUAD® Pediatric than for the comparator vaccines 3 weeks after administration of the second vaccine dose (Day 50; Table 9).

Table 9 – Immunogenicity (Heterologous Strains) of FLUAD® Pediatric in Children 6 months to <2 years of age at Day 50

	Day 50 (3 weeks after second dose)			
	FLUAD® Pediatric (aTIV) N = 132	**TIV 1 N = 216**	**TIV 2 N = 214**	**Ratios or Differences between vaccine groups**
H1N1				
GMR[a] (95% CI)	3.08 (2.54-3.75)	1.83 (1.57-2.14)	1.64 (1.41-1.92)	aTIV:TIV1 = **1.68** **(1.31-2.16)** aTIV:TIV2 = **1.88** **(1.46-2.41)**
% SC[b] (95% CI)	32 (24-40)	21 (16-27)	20 (15-26)	aTIV - TIV1 = **11** **(1.1-20.3)** aTIV - TIV2 = **12** **(2.8-21.9)**
H3N2				
GMR[a] (95% CI)	13 (10-15)	3.42 (2.93-4)	4.55 (3.9-5.32)	aTIV:TIV1 = **3.69** **(2.87-4.74)** aTIV:TIV2 = **2.78** **(2.16-3.57)**
% SC[b] (95% CI)	90 (84-95)	38 (32-45)	47 (40-54)	aTIV - TIV1 = **52** **(42.9-59.4)** aTIV - TIV2 = **43** **(34-50.9)**
B				
GMR[a] (95% CI)	22 (18-26)	4.64 (4.03-5.34)	5.34 (4.63-6.15)	aTIV:TIV1 = **4.71** **(3.75-5.93)** aTIV:TIV2 = **4.1 (3.26-5.16)**
% SC[b] (95% CI)	96 (91-99)	44 (38-51)	46 (39-53)	aTIV - TIV1 = **52** **(44.2-59)** aTIV - TIV2 = **50** **(42.1-57.1)**

[a] GMR = geometric mean ratio = Ratio of Day 50:Day 1 geometric mean titres; [b] SC = seroconversion or significant increase = the percentage of subjects achieving ≥4-fold increase in HI titre from a seropositive pre-vaccination titre (≥10), or, an HI titre ≥40 from a seronegative (<10) pre-vaccination titre. Vaccine group ratios adjusted for baseline titre. **Bold** indicates higher HI antibody response in favour of the FLUAD® Pediatric group. TIV 1= Novartis licensed subunit vaccine, TIV 2= Sanofi licensed split vaccine.

Table 10 – Immunogenicity (Heterologous Strains) of FLUAD® Pediatric in Children 6 months to <2 years of age at Day 209

	Day 209 (6 months after second dose)			
	FLUAD® Pediatric (aTIV) N = 132	**TIV 1 N = 216**	**TIV 2 N = 214**	**Ratios or Differences between vaccine groups**
H1N1				
GMR[a] (95% CI)	1.48 (1.31-1.67)	1.33 (1.21-1.46)	1.24 (1.13-1.37)	aTIV:TIV1 = 1.11 (0.95-1.3) aTIV:TIV2 = **1.19 (1.02-1.39)**
% SC[b] (95% CI)	16 (10-23)	11 (7-16)	6 (3-10)	aTIV - TIV1 = 5 (-1.9-13.3) aTIV - TIV2 = **10 (3.3-17.5)**
H3N2				
GMR[a] (95% CI)	2.36 (1.97-2.83)	1.45 (1.26-1.67)	1.67 (1.44-1.92)	aTIV:TIV1 = **1.63 (1.29-2.05)** aTIV:TIV2 = **1.42 (1.12-1.79)**
% SC[b] (95% CI)	24 (17-32)	13 (9-19)	16 (12-22)	aTIV - TIV1 = **11 (2.5-19.8)** aTIV - TIV2 = 8 (-1-17.1)
B				
GMR[a] (95% CI)	3.64 (3.18-4.17)	1.47 (1.32-1.63)	1.59 (1.43-1.77)	aTIV:TIV1 = **2.48 (2.09-2.95)** aTIV:TIV2 = **2.28 (1.92-2.71)**
% SC[b] (95% CI)	27 (19-35)	10 (6-15)	10 (6-15)	aTIV - TIV1 = **16 (8.2-25.3)** aTIV - TIV2 = **17 (8.5-25.6)**

[a] GMR = geometric mean ratio = Ratio of Day 50:Day 1 geometric mean titres; [b] SC = seroconversion or significant increase = the percentage of subjects achieving ≥4-fold increase in HI titre from a seropositive pre-vaccination titre (≥10), or, an HI titre ≥40 from a seronegative (<10) pre-vaccination titre. **Bold** indicates higher HI antibody response in favour of the FLUAD® Pediatric group. TIV 1= Novartis licensed subunit vaccine, TIV 2= Sanofi licensed split vaccine.

Elderly Population

Evaluation of vaccine immunogenicity was originally based on the CHMP criteria defined in the CPMP/BWP/214/96 guideline. Generally all 3 CHMP criteria were met with FLUAD® for each strain (see Table 11 below). When not all 3 criteria were met, the GMR and seroconversion/significant increase CHMP criteria were more frequently achieved with FLUAD® than with the comparator vaccine.

Table 11 – CHMP Criteria Fulfilled Against Homologous Influenza Strains After One Vaccination[a] - HI assay (PP-Population)

	V7P5		V7P8		V7P17		V7P24		V7P34	
	FLUAD® (w)	AGRIFLU®	FLUAD® (w)	AGRIFLU®	FLUAD® (w)	AGRIFLU®	FLUAD® (c)	Flushield	FLUAD® (c)	AGRIFLU®
	N=94	N=97	N=100	N=99	N=147	N=150	N=140	N=140	N=211	N=106
H3N2	3/3	3/3	3/3	2/3	3/3	3/3	3/3	3/3	1/3	1/3
H1N1	3/3	2/3	1/3	1/3	3/3	2/3	2/3	2/3	3/3	2/3
B	3/3	2/3	3/3	2/3	3/3	3/3	3/3	2/3	3/3	2/3

Source: FLUAD®(w) = 'water' formulation (FLUAD®/MF59W.1); FLUAD®(c) = 'citrate' formulation (FLUAD®/MF59C.1); Note: for all studies only results with FLUAD® (single syringe) are presented;
[a]i.e., on day 28.

In all five pivotal clinical trials consistent numerically higher HI antibody titers (i.e., day 28 GMT FLUAD®/comparator ratio >1) and greater percentages of subjects achieving seroconversion or significant increase in HI titres (i.e., vaccine group difference for the seroconversion rate of FLUAD®/comparator >0) for homologous strains were observed for FLUAD®. The differences were statistically significant for some strains and/or some endpoints (see Table 12 and Table 13). However, clinical relevance of the difference is unknown.

Table 12 – Postvaccination GMTs and Vaccine Group Ratios - HI assay (PP-Population)

Study	Antigen	FLUAD®		Comparator		
		N	GMT (95% CI)	N	GMT (95% CI)	Vaccine Group Ratio (99.17% CI)[#]
V7P5	H3N2	94	331 (271-406)	97	161 (132-196)	2.06 (1.4-3.03) [§]
	H1N1	94	252 (214-297)	97	179 (152-211)	1.41 (1.03-1.92) [§]
	B	94	137 (115-162)	97	85 (71-100)	1.62 (1.17-2.24) [§]
V7P8	H3N2	100	121 (69-210)	99	62 (37-104)	1.94 (1.25-3.01) [§]
	H1N1	100	179 (121-265)	99	153 (106-220)	1.17 (0.86-1.6)
	B	100	77 (52-115)	99	60 (41-86)	1.3 (0.95-1.78)
V7P17	H3N2	147	276 (228-335)	150	153 (127-185)	1.81 (1.25-2.61) [§]
	H1N1	147	367 (314-429)	150	266 (228-311)	1.38 (1.03-1.85) [§]
	B	147	289 (250-335)	150	206 (178-238)	1.41 (1.07-1.86) [§]
V7P24	H3N2	140	251 (213-295)	140	204 (173-240)	1.23 (0.9-1.68)
	H1N1	140	223 (183-272)	140	217 (178-266)	1.03 (0.7-1.5)
	B	140	182 (149-222)	140	133 (109-162)	1.37 (0.94-2.0)
V7P34	H3N2	211	243 (220-267)	106	203 (177-233)	1.19 (0.95-1.5)
	H1N1	211	203 (175-235)	106	155 (126-190)	1.31 (0.93-1.85)
	B	211	168 (147-191)	106	140 (116-168)	1.2 (0.89-1.63)

2-sided 99.17% Bonferroni adjusted CI within each study for 6 comparisons (3 strains by 2 endpoints).
[§]indicate that if CI does not contain 1, i.e. statistically significant difference.

Table 13 – Postvaccination SC and Vaccine Group Differences - HI assay (PP-Population)

Study	Antigen	FLUAD®		Comparator		
		N	SC (95% CI)	N	SC (95% CI)	Vaccine Group Difference (99.17% CI)[#]
V7P5	H3N2	94	83 (74-90)	97	61 (50-71)	22 (5-38) [§]
	H1N1	94	32 (23-42)	97	23 (15-32)	9 (-8-26)
	B	94	52 (42-63)	97	30 (21-40)	22 (4-40) [§]
V7P8	H3N2	100	54 (44-64)	99	28 (20-38)	26 (7-42) [§]
	H1N1	100	23 (15-32)	99	11 (6-19)	12 (-2-26)
	B	100	35 (26-45)	99	27 (19-37)	8 (-10-25)
V7P17	H3N2	147	55 (47-63)	150	36 (28-44)	19 (4-33) [§]
	H1N1	147	35 (27-43)	150	23 (17-31)	11 (-3-25)
	B	147	48 (40-57)	150	33 (25-41)	16 (1-30) [§]
V7P24	H3N2	140	56 (48-65)	140	35 (27-44)	21 (6-36) [§]
	H1N1	140	26 (19-35)	140	24 (17-32)	2 (-12-16)
	B	140	41 (32-49)	140	27 (20-35)	14 (-1-28)
V7P34	H3N2	211	23(18-30)	106	18(11-27)	5 (-8-17)
	H1N1	211	40 (33-47)	106	30 (22-40)	10 (-6-24)
	B	211	41 (34-48)	106	25 (17-34)	16 (1-30) [§]

SC = seroconversion or significant increase.
# 2-sided 99.17% Bonferroni adjusted CI within each study, for 6 comparisons (3 strains by 2 endpoints).
[§] indicate that if CI does not contain 0, i.e. statistically significant difference.

Postvaccination GMTs and seroconversion rates for heterologous strains were observed to be consistently higher for FLUAD® than for AGRIFLU®. The difference was statistically significant for some strains and/or some endpoints (see Table 14).

Table 14 – GMT and Seroconversion Response to Heterologous Influenza Strains After One Vaccination [a] – Study V7P3 - HI assay (PP-Population)

		FLUAD®	AGRIFLU®	Vaccine Group Comparisons (99.17% CI)[#]
		N=39	N=35	
H3N2	GMT (95% CI)	173 (117-256)	99 (65-150)	1.75 (0.81-3.8)
	% SC (95% CI)	79 (64-91)	46 (29-63)	34 (4-58) [§]
H1N1	GMT (95% CI)	270 (200-365)	133 (97-183)	2.03 (1.12-3.67) [§]
	% SC (95% CI)	74 (58-87)	37 (21-55)	37 (7-61) [§]
B	GMT (95% CI)	200 (153-261)	105 (79-139)	1.9 (1.12-3.24) [§]
	% SC (95% CI)	92 (79-98)	69 (51-83)	24 (0-48)

SC= seroconversion or significant increase, i.e., ≥4-fold increase in HI titer from a pre-vaccination titer ≥1:10 or a rise from <1:10 to ≥1:40 in those who were serum-negative at baseline;
[a] i.e., on day 28.
2-sided 99.17% Bonferroni adjusted CI within each study, for 6 comparisons (3 strains by 2 endpoints).
[§] indicate statistically significant difference/ratio.

Seroprotection GMR and rates for heterologous strains were observed to be consistently higher for FLUAD® than for AGRIFLU® (see Table 15).

Table 15 – Seroprotection and GMR Immune Response to Heterologous Influenza Strains After One Vaccination[a] – Study V7P3 - HI assay (PP-Population)

		FLUAD®	AGRIFLU®
		N=39	N=35
H3N2	% SP (95% CI)	100 (91-100)	83 (66-93)
	GMR (95% CI)	7.86 (5.41-11)	4.08 (2.75-6.06)
H1N1	% SP (95% CI)	100 (91-100)	94 (81-99)
	GMR (95% CI)	5.32 (3.84-7.36)	2.54 (1.8-3.57)
B	% SP (95% CI)	100 (91-100)	97 (85-100)
	GMR (95% CI)	9.06 (7.08-12)	3.84 (2.96-4.99)

SP= seroprotection, i.e., HI titer ≥1:40, GMR= day 28/day 0 geometric mean titer ratio.
[a] i.e., on day 28.

14.4 Immunogenicity

See 14 CLINICAL TRIALS, Trial Design and Study Demographics and 14 CLINICAL TRIALS, Study Results.

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

Table 16 – Nonclinical Toxicology Studies

Study type, gender, and species	Route and regimen[a]	Results
Repeat dose toxicity - male and female rabbits	Two or three 0.5 mL intramuscular doses of FLUAD® two weeks apart	There were no systemic adverse effects, and FLUAD® was well tolerated locally.
Delayed contact hypersensitivity - female Guinea pigs	Intradermal 0.1 mL and topical 0.5 mL doses of FLUAD® during induction phase, and topical 0.5 mL dose of FLUAD® during challenge phase.	FLUAD® was not a skin sensitiser in Guinea pigs in this study.

[a] On a body weight basis, each dose administered to rabbits was approximately 15 times the human dose

FLUAD® has not been evaluated for reproductive and developmental toxicity, carcinogenic or mutagenic potential.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

FLUAD® Pediatric and FLUAD®

(Influenza Virus Vaccine, surface antigen, inactivated, Adjuvanted with MF59C.1)

Read this carefully before you start taking **FLUAD® Pediatric and FLUAD®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FLUAD® Pediatric and FLUAD®**.

What is FLUAD® Pediatric and FLUAD® used for?

FLUAD® Pediatric/FLUAD® is an inactivated influenza virus vaccine against influenza subtypes A and B contained in the vaccine, indicated in children 6 months to less than 2 years of age and adults 65 years of age and older.

How does FLUAD® Pediatric and FLUAD® work?

FLUAD® Pediatric/FLUAD® provides active immunization of persons 6 months to less than 2 years of age and persons 65 years of age and older against influenza disease, used to prevent people from developing influenza (the flu), or reduce flu symptoms.

Like other influenza vaccines FLUAD® Pediatric/FLUAD® causes the body to produce antibodies against the virus. This means that when your body is exposed to the flu virus, your body is able to defend itself. The antibodies stop the attacking virus. You cannot catch influenza from the vaccine, since it only contains portions of the virus, and not the whole live virus. Your body takes 2 to 3 weeks to produce antibodies after vaccination. Therefore, if you are exposed to influenza immediately before or after your vaccination, you could still develop the illness. The vaccine will not protect you against the common cold, even though some of the symptoms are similar to influenza. Influenza viruses change all the time, so different vaccines are made every year. To stay protected against influenza, you need to be re-vaccinated every year before the winter season.

It is particularly important for some groups of people to be vaccinated. These include people with certain medical conditions, elderly people, people who are likely to be exposed to the infection and people on certain medications. If you are in doubt as to whether you should be vaccinated, talk to your local health professionals.

FLUAD® Pediatric/FLUAD® follows the World Health Organisation (WHO) and National Advisory Committee on Immunization (NACI) recommendation for vaccination for the northern hemisphere for the 2025-2026 season.

What are the ingredients in FLUAD® Pediatric and FLUAD®?

Medicinal ingredients:

Influenza virus vaccine (surface antigen, inactivated) subtypes A and B (2025/2026 season).

Influenza virus surface antigens (haemagglutinin and neuraminidase), of the following strains:

A/Victoria/4897/2022 (H1N1)pdm09-like virus,

A/Croatia/10136RV/2023 (H3N2)-like virus,

B/Austria/1359417/2021-like virus.

This vaccine complies with the WHO recommendations (northern hemisphere) for the 2025/2026 season.

Non-medicinal ingredients:

Calcium chloride dihydrate, citric acid, disodium phosphate dihydrate, magnesium chloride hexahydrate, polysorbate 80, potassium chloride, potassium dihydrogen phosphate, sodium chloride, sodium citrate, sorbitan trioleate, squalene and water for injections.

May also contain trace amounts of:

Cetyltrimethylammonium bromide (CTAB), egg proteins, formaldehyde, hydrocortisone, kanamycin, or neomycin.

For a full listing of nonmedicinal ingredients see Part I of the Product Monograph.

FLUAD® Pediatric and FLUAD® comes in the following dosage forms:

Each 0.5 mL dose contains 15 micrograms of influenza virus haemagglutinin (HA) and each 0.25 mL dose contains 7.5 micrograms of influenza virus HA from each of the following 3 strains:
A/Victoria/4897/2022 (H1N1)pdm09-like virus,
A/Croatia/10136RV/2023 (H3N2)-like virus,
B/Austria/1359417/2021-like virus.

- Sterile suspension for intramuscular injection provided as one or ten single dose prefilled glass syringes (Type I), without needles.
- FLUAD® Pediatric/FLUAD® does not contain thimerosal or any other preservative.
- The syringe plunger does not contain latex and FLUAD® is considered safe for use in persons with latex allergies

Do not use FLUAD® Pediatric and FLUAD® if:

- there is a history of hypersensitivity to egg proteins or other components of the vaccine, any of the excipients or in people who have had a life-threatening reaction to previous influenza vaccination. (For a complete listing, see Dosage Forms, Strengths, Composition and Packaging).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FLUAD® Pediatric and FLUAD®. Talk about any health conditions or problems you may have, including if you or your child:

- are/is allergic to eggs or egg-products
- are/is allergic to any of the following: kanamycin and neomycin sulphate, hydrocortisone, formaldehyde, cetyltrimethylammonium bromide, or polysorbate 80
- have/has a fever, or you think you may be getting a fever
- had a serious reaction to any flu vaccine in the past
- have/has any known allergies
- have/has experienced any health problems
- are pregnant: ask your doctor for advice
- are/is currently on any medication (i.e. immunosuppressant, theophylline, anticoagulants such as warfarin)

Other warnings you should know about:

FLUAD® should not be administered to anyone with known allergies to eggs or egg products, or any

other constituent of the vaccine or to anyone who has had a life-threatening reaction to previous influenza vaccination.

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.

Immunocompromised patients may have a diminished immune response to FLUAD® Pediatric/FLUAD®.

FLUAD® may be given at the same time as other vaccines. There are no data to assess the concomitant administration of FLUAD® Pediatric with other vaccines.

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

As with any vaccine, immunization with FLUAD® may not protect 100% of individuals against influenza disease.

Immunosuppressive therapies may reduce immune response to FLUAD® Pediatric/FLUAD®.

USE IN SPECIFIC POPULATIONS

- Safety and effectiveness of FLUAD® has not been established in pregnant women and nursing mothers.
- Safety and effectiveness in children over 2 years of age and adolescents has not been established.
- Antibody responses were lower in the geriatric population than in younger adult subjects.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FLUAD® Pediatric and FLUAD®:

Overview

No interaction between FLUAD® Pediatric/FLUAD® and other vaccines or medication is known.

Drug-Drug Interactions

FLUAD® may be given at the same time as other vaccines. There are no data to assess the concomitant administration of FLUAD® Pediatric with other vaccines. FLUAD® Pediatric/FLUAD® should not be mixed with any other vaccine in the same syringe. Immunization should be carried out on separate limbs. It should be noted that the systemic adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Although a possible interaction has been suggested in the literature between influenza vaccination and the use of warfarin and theophylline, clinical studies have not shown any adverse effects attributable to these drugs in people receiving influenza vaccine. There were no studies designed to evaluate the drug interactions with FLUAD® Pediatric/FLUAD®.

How FLUAD® Pediatric and FLUAD® is given:

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection).

Usual dose:

Children 6 months to <2 years of age: A single dose of 0.25 mL.

Children 6 months to <2 years of age who have not been previously vaccinated against influenza, should receive a second dose after at least 4 weeks.

Adults aged 65 years and over: A single dose of 0.5 mL.

Immunization should be carried out by intramuscular injection only.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration of the vaccine.

Overdose:

No data are available.

If you think you, or a person you are caring for, have taken too much FLUAD® Pediatric/FLUAD®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using FLUAD® Pediatric and FLUAD®?

These are not all the possible side effects you may have when taking FLUAD® Pediatric/FLUAD®. If you experience any side effects not listed here, tell your healthcare professional.

Vaccination with FLUAD® Pediatric/FLUAD® (influenza vaccine, surface antigen, inactivated) cannot cause influenza because the vaccine does not contain live virus. Respiratory disease after vaccination represents coincidental illness unrelated to influenza vaccination.

Occasionally people have side effects with influenza vaccines. The most common of these are fever, feeling unwell, shivering, tiredness, headache, sweating, muscle joint pain, and warmth. Skin reactions include redness, swelling, pain, ecchymosis (blue/black staining of the skin) and a hardening of the skin at the injection site and itching. These reactions will normally disappear without treatment in a day or two.

In clinical studies for FLUAD® in elderly population, the most common (≥10%) adverse reactions reported were headache, muscle pain, and fatigue as well as local pain, thickening, swelling, and redness at injection site.

In clinical studies for FLUAD® Pediatric in children 6 months to <2 years, the most common (≥10%) adverse reactions reported were irritability, fever, vomiting , sleepiness, change in eating habits, diarrhea, and persistent crying as well as local redness, tenderness, and thickening at injection site.

Rarely (≤ 0.1%), neuralgia (nerve pain), paresthesia (numbness and tingling), convulsions (seizures), thrombocytopenia (a blood disorder), lymphadenopathy (swelling of the glands in the neck, armpit or groin), muscular weakness, and allergic reactions (this might include but is not limited to breathing or swallowing difficulties, or swelling in the face or skin) have been reported with influenza vaccination. In rare cases, allergic reactions may lead to shock.

Vasculitis (inflammation of blood vessels) temporarily affecting the kidneys, exudative erythema multiforme (severe skin rash), neurological disorders (affecting the nerves and brain), such as encephalomyelitis, and neuritis, injection-site cellulitis-like reaction (some cases of swelling, pain, and

redness extending more than 10 cm and lasting more than 1 week) and extensive swelling of injected limb lasting more than one week have also been rarely reported.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Seqirus UK Limited cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:

This product should be stored at 2°C to 8°C (in a refrigerator), not frozen. The syringe should be kept in the outer carton, thus protecting it from light.

FLUAD® Pediatric/FLUAD® can be administered following a 2 hour exposure at temperatures between 8° and 25°C. This is not, however, a recommendation for storage.

Do not use vaccine after the expiration date.

Keep out of reach and sight of children.

If you want more information about FLUAD® Pediatric and FLUAD®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website http://www.seqirus.ca, or by calling 1-855-358-8966.

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