

FLUCELVAX®
Trivalent inactivated influenza vaccine (subunits), developed in cell culture
Made in the USA
WHO STRAINS - 2026 SEASON - SOUTHERN HEMISPHERE
Sold under medical prescription

COMPOSITION
Each 0.5 mL contains: Active ingredients: influenza virus surface antigens (hemagglutinin and neuraminidase)*, inactivated, from the following Southern Hemisphere 2026 Season strains:
A/Missouri/11/2025 (H1N1)pdm09-like strain (A/Tasmania/318/2025 CVR-351) 15 µg hemagglutinin per dose.
A/Sydney/1359/2024 (H3N2)-like strain (A/Singapore/GP20238/2024) 15 µg hemagglutinin per dose.
B/Austria/1359417/2021 (B/Victoria lineage)-like strain (B/Singapore/WUH4618/2021) 15 µg hemagglutinin per dose.
* Propagated in Madin Darby Canine Kidney Cells (MDCK).
Excipients: sodium chloride, potassium chloride, magnesium chloride hexahydrate, disodium phosphate dihydrate, potassium dihydrogen phosphate, thimerosal, water for injections q.s. to 0.5 mL.
Each dose of FLUCELVAX® may contain residual amounts of MDCK cell protein (≤ 21.6 mcg), protein other than HA (≤ 225 mcg), MDCK cell DNA (≤ 10 ng), polysorbate 80 (≤ 11.25 mcg), cetyltrimethylammonium bromide (≤ 13.5 mcg), and β-propiolactone (< 0.5 mcg), which are used in the manufacturing process.

PHARMACEUTICAL FORM
FLUCELVAX® contains no egg protein or antibiotics. FLUCELVAX® 5 mL multi-dose vials contain thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose from the multi-dose vial contains 25 mcg mercury. The multi-dose vial stoppers are not made with natural rubber latex.
FLUCELVAX® is an injectable suspension. A single dose is 0.5 mL.

THERAPEUTIC ACTION
Anti-influenza vaccine. ATC Code (Therapeutic class): J07B B02

INDICATIONS
FLUCELVAX® is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUCELVAX® is indicated for use in persons 6 months of age and older [see CLINICAL STUDIES].

PHARMACOLOGICAL PARTICULARS / PROPERTIES
Mechanism of Action
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. In some studies, HI antibody titers of $\geq 1:40$ have been associated with protection from influenza illness in up to 50% of adults. Antibody against one influenza virus type or subtype confers little 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 strains in each year's influenza vaccine. Therefore, inactivated influenza vaccines are standardized to contain the hemagglutinin of the influenza virus strains which are representative of the influenza viruses likely to circulate in Argentina in the upcoming winter. Annual reimmunization with the current vaccine is recommended as immunity declines during the year following vaccination and circulating influenza virus strains change every year.

CLINICAL STUDIES
Efficacy in Adults
A multinational (US, Finland, and Poland), randomized, observer-blind, placebo-controlled trial was performed to assess clinical efficacy and safety of FLUCELVAX® during the 2007-2008 influenza season in adults aged 18 through 49 years (Study 5). A total of 11,404 adults were enrolled to receive FLUCELVAX® (N=3828), AGRIFLU® (N=3676) or placebo (N=3900) in a 1:1:1 ratio. Among the overall study population enrolled, the mean age was 33 years, 55% were female, 84% were Caucasian, 7% were Black, 7% were Hispanic, and 2% were of other ethnic origin.
FLUCELVAX® efficacy was assessed by the prevention of culture-confirmed symptomatic influenza illness caused by viruses antigenically matched to those in the vaccine and prevention of influenza illness caused by all influenza viruses compared to placebo. Influenza cases were identified by active and passive surveillance of influenza-like illness (ILI). ILI was defined as a fever (oral temperature $\geq 38.3^{\circ}\text{C}$) and cough or sore throat. Nose and throat swab samples were collected for analysis within 120 hours of onset of an influenza-like illness in the period from 21 days to 6 months after vaccination. Overall vaccine efficacy against all influenza viral subtypes and vaccine efficacy against individual influenza viral subtypes were calculated (Tables 1 and 2, respectively).

Table 1: Vaccine Efficacy against Culture-Confirmed Influenza in Participants aged 18 through 49 years (Study 5)

	Number of participants per protocol	Number of participants with influenza	Attack Rate (%)	Vaccine Efficacy (VE) ^{1,2}	
				%	Lower Limit of One-Sided 97.5% CI of VE ³
Antigenically Matched Strains					
FLUCELVAX®	3776	7	0.19	83.8	61.0
Placebo	3843	44	1.14	—	—
All Culture-Confirmed Influenza					
FLUCELVAX®	3776	42	1.11	69.5	55.0
Placebo	3843	140	3.64	—	—

¹ Efficacy against influenza was evaluated over a 9-month period in 2007/2008. ² Simultaneous one-sided 97.5% confidence intervals for the vaccine efficacy (VE) of FLUCELVAX® relative to placebo based on the Sidak-corrected score confidence intervals for the relative risk. Vaccine Efficacy = (1 - Relative Risk) \times 100%. ³ VE success criterion: the lower limit of the one-sided 97.5% CI for the estimate of the VE relative to placebo is $\geq -40\%$.

Study 5: NCT00630331

Table 2: Efficacy of FLUCELVAX® against Culture-Confirmed Influenza by Influenza Viral Subtype in Participants aged 18 through 49 years (Study 5)

	FLUCELVAX® (N=3776)		Placebo (N=3843)		Vaccine Efficacy (VE) ^{1,2}	
	Attack Rate (%)	Number of Participants with Influenza	Attack Rate (%)	Number of Participants with Influenza	%	Lower Limit of One-Sided 97.5% CI of VE ³
Antigenically Matched Strains						
A/H3N2 ⁴	0.05	2	0	0	—	—
A/H1N1	0.13	5	1.12	43	88.2	67.4
B	0	0	0.03	1	—	—
All Culture-Confirmed Influenza						
FLUCELVAX®	0.16	6	0.65	25	75.6	35.1
AGRIFLU®	0.16	6	1.48	57	89.3	73.9
Placebo	0.76	30	3.59	61	49.3	18.2

¹ VE success criterion was prespecified in the protocol for each influenza virus subtype. ² Simultaneous one-sided 97.5% confidence intervals for the vaccine efficacy (VE) of FLUCELVAX® relative to placebo based on the Sidak-corrected score confidence intervals for the relative risk. Vaccine Efficacy = (1 - Relative Risk) \times 100%. ³ There were too few cases of influenza due to vaccine-matched influenza A/H3N2 or B to adequately assess vaccine efficacy.

Study 5: NCT00630331

Efficacy in Children and Adolescents

Absolute efficacy of FLUCELVAX® QUADRIVALENT was evaluated in children and adolescents 2 through 17 years of age in Study 4. This was a multinational, randomized, non-influenza vaccine comparator-controlled efficacy, immunogenicity and safety study conducted in 8 countries during the following 3 influenza seasons: Southern Hemisphere 2017, Northern Hemisphere 2017/2018 and Northern Hemisphere 2018/2019. The study enrolled 4514 children and adolescents. Out of the 4514 enrolled, 4513 received either FLUCELVAX® QUADRIVALENT (N=2258) or a non-influenza comparator vaccine (N=2256) (A/Cyprus/10/2015 (H1N1)pdm09-like strain (A/Sydney/05/2015) oligosaccharide diptheria CRM197 conjugated vaccine (N=2255). The full analysis set (FAS) for efficacy consisted of 4509 children and adolescents. Data for FLUCELVAX® QUADRIVALENT are relevant to FLUCELVAX® because both vaccines are manufactured using the same process and have overlapping compositions.
Children 2 through 8 years of age received either one or two doses (separated by 4 weeks) of FLUCELVAX® QUADRIVALENT or comparator vaccine depending on the subject's prior influenza vaccination history. Children in the 2-dose comparator group received non-influenza comparator as the first dose and saline placebo as the second dose. Children and adolescents 9 through 17 years of age received a single dose of FLUCELVAX® QUADRIVALENT or non-influenza comparator vaccine. Among all enrolled children and adolescents (N=4514), the mean age was 8.3 years, 48% were female, 51% were 2 through 8 years of age, 50% were Caucasian and 49% were Asian. There were no notable differences in the distribution of demographic and baseline characteristics between the two treatment groups.

FLUCELVAX® QUADRIVALENT efficacy was assessed by the prevention of confirmed influenza illness caused by any influenza Type A or B strain. Influenza cases were identified by active and passive surveillance of influenza-like illness (ILI) and confirmed by cell culture and/or real-time polymerase chain reaction (RT-PCR). ILI was defined as a fever (oral temperature $\geq 37.8^{\circ}\text{C}$) along with any of the following: cough, sore throat, nasal congestion, or rhinorrhea. The overall vaccine efficacy for the entire study population (2 through 17 years) was 54.6% (95% CI 45.7 – 62.1), which met predefined success criteria. In addition, vaccine efficacy was 50.5% (95% CI 38.4 – 60.2) in children 2 through 8 years of age and 61.9% (95% CI 47.4 – 72.3) in those 9 through 17 years of age. Vaccine efficacy against all influenza viral subtypes and against individual influenza viral subtypes antigenically similar to the subtypes in the vaccine were calculated (Table 3).

Table 3: Efficacy of FLUCELVAX® QUADRIVALENT Against First Occurrence RT-PCR Confirmed or Culture Confirmed Influenza in Participants 2 through 17 years of age – FAS Efficacy (Study 4).

	Number of participants per protocol ¹	Number of cases of influenza	Attack Rate (%)	Vaccine Efficacy (VE) ²	
				VE %	95% Confidence Interval ³
RT-PCR or Culture Confirmed Influenza					
FLUCELVAX® QUADRIVALENT	2257	175	7.8	54.6	45.7 – 62.1
Non-Influenza Comparator ⁴	2252	364	16.2	-	-
Culture Confirmed Influenza					
FLUCELVAX® QUADRIVALENT	2257	115	5.1	60.8	51.3 – 68.5
Non-Influenza Comparator ⁴	2252	279	12.4	-	-
Antigenically Matched Culture-Confirmed Influenza					
FLUCELVAX® QUADRIVALENT	2257	90	4.0	63.6	53.6 – 71.5
Non-Influenza Comparator ⁴	2252	236	10.5	-	-

¹ Number of participants in the Full-Analysis Set (FAS) – Efficacy, which included all participants randomized, received a study vaccination and provided efficacy data. ² Efficacy against influenza was evaluated over three influenza seasons, SH 2017, NH 2017-18 and NH 2018-19. ³ FLUCELVAX® QUADRIVALENT met the pre-defined success criterion defined as the lower limit of the two-sided 95% CI of absolute vaccine efficacy greater than 20%. ⁴ Non-Influenza Comparator (MENVEO, meningococcal (Groups A, C, Y, and W-135) oligosaccharide diptheria CRM197 conjugate vaccine, GlaxoSmithKline Biologicals SA); children assigned to 2 doses received saline placebo as the second dose.

Study 4: NCT01365617

Immunogenicity in Adults

Immunogenicity in adults 18 years of age and older was evaluated in clinical Study 6, a randomized, active controlled, multicenter study conducted in Poland during the 2016/2017 Southern Hemisphere influenza season. In this study, immunogenicity was assessed 3 weeks after vaccination in 2640 subjects who received either FLUCELVAX® (N=1322) or the egg-based trivalent influenza comparator, AGRIFLU® (N=1318). Among the overall study population enrolled, 59% were female, 100% of subjects were Caucasian, and the mean age was 43.5 years.
In Study 6, non-inferiority of FLUCELVAX® to AGRIFLU® was demonstrated for HI antibody responses to all three strains for both post-vaccination geometric mean titer (GMT) ratios and seroconversion rates. Success for non-inferiority of the GMT ratio was defined as the lower limit of the two-sided 95% CI for GMT ratio (FLUCELVAX®/AGRIFLU®) >0.67 , and success for non-inferiority of seroconversion rate was defined as the lower limit of the two-sided 95% CI for the difference between the seroconversion rates (FLUCELVAX® – AGRIFLU®) was $\geq -10\%$ (Table 4).

Table 4: Non-inferiority Analysis of FLUCELVAX® to a US-Licensed Comparator in Adults 18 through 49 Years and 50 through 64 Years of Age (Study 6)

	Ratio or Difference (95% CI): FLUCELVAX® Versus Comparator ²					
	A/H1N1		A/H3N2		B	
Subjects 18 through 49 Years: N FLUCELVAX®=478; N comparator=472						
GMTs ratio ^{1,4}	0.96		0.98		1.07	
(FLUCELVAX® / AGRIFLU)	(0.81, 1.13)		(0.87, 1.11)		(0.93, 1.23)	
Difference in Seroconversion Rates ^{1,5,6}	2%		2%		5%	
(FLUCELVAX® – AGRIFLU)	(-4.8)		(-5.8)		(1.10)	
Subjects 50 through 64 Years: N FLUCELVAX®=340; N comparator=365						
GMTs ratio ^{1,4}	0.96		0.87		1.23	
(FLUCELVAX® / AGRIFLU)	(0.79, 1.16)		(0.74, 1.02)		(1.02, 1.48)	
Difference in Seroconversion Rates ^{1,5,6}	1%		-2%		3%	
(FLUCELVAX® – AGRIFLU)	(-6.8)		(-9.5)		(-4.9)	

¹ NCT0492063. ² AGRIFLU (Influenza Virus Vaccine). ³ Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval (CI) for geometric mean titer (GMT) ratio (FLUCELVAX®/AGRIFLU) was >0.67 . ⁴ Egg derived antigen hemagglutination inhibition (HI) assay results. ⁵ Rates of seroconversion = percentage of subjects with either a pre-vaccination HI titer $< 1:10$ and a post-vaccination HI titer $\geq 1:40$ or a pre-vaccination HI titer $\geq 1:10$ and at least a four-fold rise in post-vaccination HI antibody titer.

⁶ Non-inferiority was demonstrated if the lower limit of two-sided 95% confidence interval (CI) for difference in percentages of subjects with seroconversion (FLUCELVAX® – AGRIFLU) was $\geq -10\%$.
Non-inferiority of FLUCELVAX® to AGRIFLU® was demonstrated for HI antibody responses to all three strains for both post-vaccination GMT ratios and seroconversion rates. Success for non-inferiority of the GMT ratio was defined as the lower limit of the two-sided 95% CI for the GMT ratio (FLUCELVAX® / AGRIFLU®) >0.67 , and success for non-inferiority of seroconversion rate was defined as the lower limit of the two-sided 95% CI for the difference between the seroconversion rates (FLUCELVAX® – AGRIFLU®) $\geq -10\%$ (Table 5).

Table 5: Non-inferiority Analysis of FLUCELVAX® to a US-Licensed Comparator in Adults 65 Years of Age and Older (Study 6)

	Ratio or Difference (95% CI): FLUCELVAX® Versus Comparator ² (N FLUCELVAX®=504; N comparator=481)		
	A/H1N1	A/H3N2	B
	(N FLUCELVAX®=504; N comparator=481)		
GMTs ratio ^{1,4} (FLUCELVAX® / AGRIFLU)	1.06 (0.92, 1.22)	0.97 (0.84, 1.12)	1.28 (1.11, 1.48)
Difference in Seroconversion Rates ^{1,5} (FLUCELVAX® – AGRIFLU)	-1% (-7.6)	3% (-2.9)	7% (1.12)

¹ NCT0492063. ² AGRIFLU (Influenza Virus Vaccine). ³ Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval (CI) for geometric mean titer (GMT) ratio (FLUCELVAX®/AGRIFLU) was >0.67 . ⁴ Egg derived antigen hemagglutination inhibition (HI) assay results. ⁵ Rates of seroconversion = percentage of subjects with either a pre-vaccination HI titer $< 1:10$ and a post-vaccination HI titer $\geq 1:40$ or a pre-vaccination HI titer $\geq 1:10$ and at least a four-fold rise in post-vaccination HI antibody titer.

Immunogenicity in Children

Immunogenicity in children 6 months through 3 years of age was evaluated in a randomized, observer-blind, multicenter study conducted in the US (Study 1). In this study, subjects received FLUCELVAX® QUADRIVALENT or a US-licensed comparator quadrivalent influenza vaccine (FLUCELVAX® QUADRIVALENT N=1557, comparator QUADRIVALENT (QIV) N=805). In the per protocol set, the mean age of subjects who received FLUCELVAX® QUADRIVALENT was 25 months; 49% of subjects were female and 67% of subjects were Caucasian, 27% were Black and $< 1\%$ were Asian, Hawaiian or other Pacific Islander and American Indian or Alaska Native. Twenty six percent of subjects were of Hispanic origin. The immune response to each of the vaccine antigens was assessed 28 days after last vaccination.

The immunogenicity endpoints were geometric mean antibody titers (GMTs) and percentage of subjects who achieved seroconversion, defined as a pre-vaccination HI or microneutralization (MNI) titer of $< 1:10$ with a post-vaccination titer $\geq 1:40$ or with a pre-vaccination HI or MNI titer $\geq 1:10$ and a minimum 4-fold increase in serum antibody titer. GMTs and seroconversion rates were measured by hemagglutination inhibition (HI) assay for A/H1N1, B/Yamagata and B/Victoria strains and by microneutralization (MNI) assay for the A/H3N2 strain.
FLUCELVAX® QUADRIVALENT was noninferior to the Comparator QIV. Noninferiority was established for all 4 influenza strains as assessed by ratios of GMTs and the differences in the percentages of subjects achieving seroconversion at 4 weeks following vaccination.
The noninferiority data observed are summarized in Table 6.

Table 6: Noninferiority¹ of FLUCELVAX® QUADRIVALENT Relative to Comparator QIV in Children 6 Months through 3 Years of Age – Per-Protocol Analysis Set² (Study 1)

	FLUCELVAX® QUADRIVALENT		Comparator QIV		Vaccine Group Ratio		Vaccine Group Difference	
	N=1092	N=575	N=575	N=575				
A/H1N1 ¹	GMT (95% CI)	79.0 (70.75, 86.03)	57.3 (50.76, 64.63)	0.73 (0.65, 0.84)	0.73	-	-	-
	Seroconversion Rate ¹ (95% CI)	58.24% (55.25, 61.19)	46.78% (42.84, 50.56)	-	-	-	-11.46 (-16.45, -6.42)	-
	N	1073	572	-	-	-	-	-
A/H3N2 ¹	GMT (95% CI)	23.1 (21.21, 25.12)	23.9 (21.57, 26.57)	1.04 (0.93, 1.16)	1.04	-	-	-
	Seroconversion Rate ¹ (95% CI)	27.64% (24.99, 30.42)	30.77% (27.83, 34.73)	-	-	-	3.13 (-1.46, 7.81)	-
	N	1092	575	-	-	-	-	-
B/Yamagata ¹	GMT (95% CI)	35.6 (32.93, 38.58)	26.0 (23.54, 28.43)	0.73 (0.66, 0.81)	0.73	-	-	-
	Seroconversion Rate ¹ (95% CI)	31.52% (43.53, 49.53)	27.37% (27.37, 35.63)	-	-	-	-14.87 (-19.61, -9.98)	-
	N	1092	575	-	-	-	-	-
B/Victoria ¹	GMT (95% CI)	22.4 (20.73, 24.19)	19.6 (17.81, 21.58)	0.88 (0.79, 0.97)	0.88	-	-	-
	Seroconversion Rate ¹ (95% CI)	30.31% (27.60, 33.13)	24.35% (20.89, 28.07)	-	-	-	-5.96 (-10.33, -1.44)	-
	N	1092	575	-	-	-	-	-

Abbreviations: GMT = geometric mean titer; CI = confidence interval.

Assays: GMTs and seroconversion rates were measured by hemagglutination inhibition (HI)¹ assay for A/H1N1, B/Yamagata and B/Victoria strains and by microneutralization (MNI)² assay for the A/H3N2 strain, using cell-derived target tissues. The MNI assay was used for A/H3N2 as circulating strains indicated a reduced ability to agglutinate red blood cells. FLUCELVAX® QUADRIVALENT was noninferior to the Comparator QIV irrespective of the assay used. HI assay data for A/H3N2: GMT (95%CI) for FLUCELVAX® QUADRIVALENT (N=1089) = 288.1 (261.46, 317.54), Comparator QIV (N=575) = 227.6 (201.87, 256.58), Vaccine group ratio (95%CI) = 0.79 (0.69, 0.90), Seroconversion rate (95%CI) for FLUCELVAX® QUADRIVALENT (N=1089) = 72.27% (69.51/74.91), Comparator QIV (N=575) = 64.52% (60.46, 68.44), Vaccine Group Difference (95%CI) = -7.75% (-12.51, -3.06).

Success criteria: The upper bound of the two-sided 95% confidence interval (CI) on the ratio of the GMTs (calculated as GMT US-licensed comparator QIV divided by GMT FLUCELVAX® QUADRIVALENT) did not exceed 1.5. The upper bound of the two-sided 95% CI on the difference between the seroconversion rates (calculated as Seroconversion rate US-licensed comparator QIV minus Seroconversion rate FLUCELVAX® QUADRIVALENT) did not exceed 10%.

¹ Analyses are performed on data for Day 29 for previously vaccinated subjects and Day 57 for not previously vaccinated subjects. ² Per protocol set: All participants in Full Analysis Set, immunogenicity population, who have correctly received the assigned vaccine, have no major protocol deviations leading to exclusion as defined prior to unblinding/analysis and are not excluded due to other reasons defined prior to unblinding or analysis. ³ Seroconversion rate = percentage of subjects with either a pre-vaccination titer $< 1:10$ and post-vaccination titer $\geq 1:40$ or with a pre-vaccination titer $\geq 1:10$ and a minimum 4-fold increase in post-vaccination titer.

Study 1: NCT 04074928

POSOLOGY/DOSAGE METHOD OF ADMINISTRATION

Route of Administration

For intramuscular injection only.

Dosage and Schedule

Administer FLUCELVAX® as a single 0.5 mL dose, preferably in the deltoid muscle region of the upper arm. The suggested vaccination site for infants and young children with insufficient deltoid muscle mass is the anterolateral thigh. Do not inject the vaccine into the gluteal region or areas where a central nervous trunk may be present.

Table 7: Dosage and Schedule

Age	Dose	Schedule
6 months through 8 years of age	One or two doses ¹ , 0.5 mL each	If 2 doses, administer at least 4 weeks apart
9 years of age and older	One dose, 0.5 mL	Not Applicable

¹ Children 6 months to < 9 years of age not previously vaccinated against influenza should receive a second dose.

Method of Administration

Shake the multi-dose vial preparation each time before withdrawing a dose of vaccine. FLUCELVAX® is a slightly opalescent suspension. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. If either condition exists, do not administer the vaccine. Between uses, return