Fluvax®

WARNING: This season's vaccine is indicated for use only in persons aged 5 years and over. It must not be used in children under 5 years (see Contraindications). It should only be used in children aged 5 to under 9 years based on a careful consideration of potential risks and benefits in the individual (see Precautions).

For season 2017

Name of the Medicine

Fluvax® vaccine
Inactivated influenza vaccine (split virion)
Suspension for injection

Description

This is a purified, inactivated, split virion (split virus) vaccine each 0.5 mL of which contains antigens representative of the following types:

A/Singapore/GP1908/2015 (IVR-180) (A/Michigan/45/2015 (H1N1) – like):
15 µg haemagglutinin per dose
A/Hong Kong/4801/2014 (NYMC X-263B) (A/Hong Kong/4801/2014 (H3N2) – like):
15 µg haemagglutinin per dose
B/Brisbane/46/2015 (B/Brisbane/60/2008 - like):
15 µg haemagglutinin per dose

Each 0.5 mL dose also contains, nominally: sodium chloride 4.1 mg, dibasic sodium phosphate anhydrous 0.3 mg, monobasic sodium phosphate 0.08 mg, potassium chloride 0.02 mg, monobasic potassium phosphate 0.02 mg and calcium chloride 1.5 µg.

Trace amounts of the following may also be present in each 0.5 mL dose: sodium taurodeoxycholate, ovalbumin (<1 µg), sucrose, neomycin, polymyxin B sulfate and propiolactone.

The type and amount of viral antigens in Fluvax® vaccine conform to the requirements of the Australian Influenza Vaccine Committee and the New Zealand Ministry of Health for the winter of 2017. The strains chosen for vaccine manufacture are endorsed by the Australian Influenza Vaccine Committee as being antigenically equivalent to the reference virus.

The vaccine is prepared from virus grown in the allantoic cavity of embryonated eggs, purified by zonal centrifugation, inactivated by propiolactone and disrupted by sodium taurodeoxycholate. Fluvax® vaccine conforms in safety and sterility to the requirements of the British Pharmacopoeia.

Fluvax® vaccine is a clear to slightly opaque liquid with some sediment that resuspends upon shaking.
See Administration.

Pharmacology

Fluvax® vaccine has been shown to induce antibodies to the viral surface glycoproteins, haemagglutinin and neuraminidase. These antibodies are important in the prevention of natural infection.

Seroprotection is generally obtained within 2 to 3 weeks. The duration of post vaccination immunity to homologous strains or to strains closely related to the vaccine strains varies, but is usually 6 to 12 months.

Indications

For the prevention of influenza caused by Influenza Virus, Types A and B. For the Southern Hemisphere 2017 season, the vaccine is indicated for use only in persons aged 5 years and over.
See Precautions and Dosage and Administration.

For full details regarding recommendations for influenza vaccination, please refer to the relevant national immunisation guidelines.

Contraindications

Fluvax® vaccine must not be used in children under 5 years.

Hypersensitivity to previous influenza vaccination or to egg protein, neomycin, polymyxin B sulfate or any of the constituents or trace residues (see Description section) of this vaccine.

Immunisation must be postponed in people who have febrile illness or acute infection.

Precautions

During the 2010 Southern Hemisphere influenza season, there was an unexpected increase in reports of fever and febrile convulsions in children aged less than 5 years following seasonal influenza vaccination. Febrile convulsions were reported uncommonly (i.e. reporting frequency estimated to be in the range ≥ 1/1000 to < 1/100)*. The vaccine is only indicated for use for Southern Hemisphere season 2017 in persons aged 5 years and over.
(*estimated from epidemiological investigations)
See Indications and Dosage and Administration.

Febrile events were also observed in children aged 5 to under 9 years. Therefore in this age group a decision to vaccinate with the 2017 Southern Hemisphere formulation of Fluvax® vaccine should be based on careful consideration of potential benefits and risks in the individual.

As with other injectable vaccines, appropriate medical treatment and supervision should always be available in case of anaphylactic reactions. Adrenaline should always be ready for immediate use whenever any injection is given.

Minor illness with or without fever should not contraindicate the use of influenza vaccine.

In immunocompromised patients (including those undergoing corticosteroid or immunosuppressant treatment), the antibody response may be lower.

If Guillain-Barré syndrome has occurred within 6 weeks of previous influenza vaccination, the decision to give Fluvax® vaccine should be based on careful consideration of the potential benefits and risks.

Use in Pregnancy: Category B2

It is recommended that influenza immunisation be offered in advance to women planning a pregnancy, and to pregnant women who will be in the second or third trimester during the influenza season, including those in the first trimester at the time of vaccination. The vaccine has not been evaluated in pregnant women.

An animal reproduction study has been conducted with CSL Influenza Vaccine. This study did not demonstrate any maternal or developmental toxicity.

Use in Lactation:

The vaccine has not been evaluated in nursing mothers.

Interactions with other Medicines

Fluvax® vaccine can be administered concurrently with other vaccines, however separate syringes and a separate arm should be used.

Adverse Effects

Clinical trials:

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

Paediatric studies
In clinical studies, CSL Influenza Vaccine has been administered to, and safety information collected for, 3,009 children aged 6 months to < 18 years. Clinical safety data for CSL Influenza Vaccine in children is presented from 3 clinical studies which include a randomised, observer-blind, comparator-controlled study (CSLCT-USF-07-36; 2009/2010 Northern Hemisphere vaccine formulation) and 2 open label, uncontrolled studies (CSLCT-USF-06-29; 2009 Southern Hemisphere vaccine formulation and CSLCT-FLU-04-05; Primary vaccination with the 2005 Southern Hemisphere vaccine formulation and 12 month follow up with the 2006 Southern Hemisphere vaccine formulation). Participants aged 6 months to < 9 years received one or two vaccinations as determined by previous vaccination history, with each vaccination a 0.25 mL dose for participants aged 6 months to < 3 years and a 0.5 mL dose for participants aged ≥ 3 years to < 9 years.

The safety assessment was similar for the paediatric studies with local (injection site) adverse reactions and systemic adverse events solicited for 7 days after vaccination and unsolicited adverse events collected for 30 days after vaccination. All adverse events are presented regardless of any treatment causality assigned by study investigators.

In the comparator-controlled study (CSLCT-USF-07-36), the incidence of any fever in children 6 months to < 3 years of age following the first and second doses of CSL Influenza Vaccine was 37% and 15%, respectively, as compared to 14% following each dose in the comparator group. The incidence of moderate or severe fever (≥39°C) in children 6 months to < 3 years of age following the first and second doses of CSL Influenza Vaccine was 16% and 3%, respectively, as compared to 4% and 4% following each dose in the comparator group. Among children 3 years to < 5 years of age, the incidence of any fever following the first and second doses of CSL Influenza Vaccine was 32% and 14%, respectively, as compared to 11% and 16% in the comparator. The incidence of moderate or severe fever (≥39°C) in children 3 to < 5 years of age following the first and second doses of CSL Influenza Vaccine was 15% and 3%, respectively, as compared to 1% and 0% following each dose in the comparator group.

In an open-label study (CSLCT-USF-06-29), fever, irritability, loss of appetite, and vomiting/diarrhoea occurred more frequently in children 6 months to < 3 years of age as compared to older children. Across three paediatric studies (CSLCT-USF-07-36, CSLCT-USF-

06-29 and CSLCT-FLU-04-05), 1.2% of eligible children (n=1,764) were discontinued from the second vaccination because of severe fever (≥ 40ºC) within 48 hours of the first vaccination. Across the three paediatric studies, two children, a 7-month old and a 3-year old, experienced vaccine-related febrile convulsions (rate of 0.07% across studies), one of which was serious.

Data from these studies are presented in Tables 1 and 2 for children 5 years of age and older, consistent with the currently approved age indication. See Precautions for risks of CSL Influenza Vaccine in children less than 5 years of age. Among the paediatric studies, there were no vaccine-related deaths or vaccine-related serious adverse events reported in children 5 years of age and older. Following a single 12 month follow up dose of CSL Influenza Vaccine (2006 southern hemisphere vaccine formulation study CSLCT-FLU-04-05), in participants aged 5 to < 9 years the incidence of pain was 77%, redness 53%, swelling 32%, fever 13% and vomiting/diarrhoea 6%.

Table 1: Proportion of Paediatric Subjects Aged 5 to < 18 Years with Solicited Local Adverse Reactions or Systemic Adverse Events within 7 Days after Administration of First or Second Dose of CSL Influenza Vaccine, Irrespective of Causality (CSLCT-USF-07-36)

	Percentage [a] of Subjects in each Age Group Reporting Event			
	≥ 5 to < 9 years		**≥ 9 to < 18 years**	
	CSL Influenza Vaccine N = 161 [b]	**Comparator N = 165** [b]	**CSL Influenza Vaccine N = 254** [b]	**Comparator N = 250** [b]
Post dose 1				
Local Adverse Reactions				
Pain	63	60	66	60
Redness	23	27	17	17
Induration	17	17	15	16
Systemic Adverse Events				
Myalgia	34	30	40	37
Malaise	24	13	22	20
Headache	21	19	27	26
Any Fever Fever ≥39°C	16 5	8 1	6 3	4 1
Nausea/Vomiting	12	8	9	10
Diarrhoea	7	7	8	10
	CSL Influenza Vaccine N = 39 [b]	**Comparator N = 53** [b]		
Post dose 2				
Local Adverse Reactions				
Pain	36	38	-	-
Redness	10	19	-	-
Induration	8	17	-	-
Systemic Adverse Events				
Diarrhoea	13	6	-	-
Headache	13	13	-	-
Myalgia	13	17	-	-
Malaise	5	8	-	-
Nausea/Vomiting	3	8	-	-
Any Fever Fever ≥39°C	0 0	2 0	- -	- -

[a] Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).
[b] N = number of subjects in the Safety Population for each treatment group.

Table 2: Proportion of Paediatric Subjects Aged 5 to < 18 Years of Age with Solicited Local Adverse Reactions or Systemic Adverse Events within 7 Days after Administration of CSL Influenza Vaccine, Irrespective of Causality (Studies CSLCT-USF-06-29 and CSLCT-FLU-04-05)

	Percentage [a] of Subjects in each Age Group Reporting Event		
	CSLCT-USF-06-29 and CSLCT-FLU-04-05 ≥ 5 to < 9 years		CSLCT-USF-06-29 ≥ 9 to < 18 years
	Dose 1 N = 82 - 595 [b]	Dose 2 N = 82 - 426 [b]	Dose 1 N = 397 [b]
Local Adverse Reactions			
Pain	61	56	68
Erythema	24	23	17
Swelling	17	17	13
Systemic Adverse Events			
Irritability [d]	18	16	-
Headache	16	10	27
Malaise or feeling generally unwell [c]	16	8	17
Any Fever Fever ≥39°C	13 3	6 2	5 1
General Muscle Ache (Myalgia)	12	8	20
Nausea/Vomiting [c]	7	3	5
Vomiting/Diarrhoea [d]	5	6	-
Loss of appetite [d]	5	4	-
Diarrhoea [c]	4	2	5

[a] Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

[b] N = number of subjects in the Safety Population for each treatment group. For the ≥ 5 to < 9 years age group denominators for Dose 1 were: N=82 for Vomiting/Diarrhoea, Irritability, Loss of appetite, N=513 for Malaise, Diarrhoea, Nausea/Vomiting and N=593-595 for all other parameters. Denominators for Dose 2 were: N=82 for Vomiting/Diarrhoea, Irritability, Loss of appetite, N=344 for Malaise, Diarrhoea and Nausea/Vomiting and N=421-426 for all other parameters.

[c] These preferred terms were used to describe Solicited Adverse Events in Study CSLCT-USF-06-29.
[d] These preferred terms were used to describe Solicited Adverse Events in Study CSLCT-FLU-04-05.

In Study CSLCT-USF-07-36, unsolicited adverse events that occurred in ≥ 5% of participants aged 5 to < 9 years who received CSL Influenza Vaccine following the first or second dose included cough (15%) and pyrexia (9%). Unsolicited adverse events that occurred in ≥ 5% of participants aged 9 to < 18 years who received CSL Influenza Vaccine following the first dose included cough (7%), oropharyngeal pain (7%), headache (7%) and nasal congestion (6%).

In Studies CSLCT-USF-06-29 and CSLCT-FLU-04-05, unsolicited adverse events that occurred in ≥ 5% participants aged 5 to < 9 years after the first or second dose included the following: upper respiratory tract infection (13%), cough (10%), rhinorrhoea (7%), headache (5%), nasopharyngitis (5%) and pyrexia (5%). Unsolicited adverse events that occurred in ≥ 5% of participants aged 9 to < 18 years who received CSL Influenza Vaccine following the first dose included upper respiratory tract infection (9%) and headache (8%).

Adult studies

In clinical studies, a single dose of CSL Influenza Vaccine was administered to, and safety information collected for, 11,104 adults (≥ 18 to < 65 years) and 630 older adults (≥ 65 years). Clinical data in adults is presented from 3 clinical studies which include 2 randomised, observer-blind, placebo-controlled studies in adults (CSLCT-FLU-05-09, 2006 Southern Hemisphere vaccine formulation; and CSLCT-USF-06-28, 2008 and 2009 Southern Hemisphere vaccine formulations) and one randomised, observer-blind, comparator-controlled study in older adults (CSLCT-USF-07-41, 2008/2009 Northern Hemisphere vaccine formulation). In all adult studies, there were no vaccine-related deaths or vaccine-related serious adverse events reported.

The safety assessment was identical for the three adult studies, with local (injection-site) adverse reactions and systemic adverse events solicited for 5 days after vaccination (Table 3). Unsolicited adverse events were collected for 21 days after vaccination. All adverse events are presented regardless of any treatment causality assigned by study investigators.

Table 3: Proportion of Adult and Older Adult subjects 18 Years of Age and Older with Solicited Local Adverse Reactions or Systemic Adverse Events within 5 Days after Administration of CSL Influenza Vaccine or Placebo, Irrespective of Causality (Studies CSLCT-FLU-05-09, CSLCT-USF-06-28 and CSLCT-USF-07-41)

	Percentage [a] of Subjects in each Age Group Reporting Event					
	CSLCT-FLU-05-09 [c] ≥ 18 to < 65 years		CSLCT-USF-06-28 ≥ 18 to < 65 years		CSLCT-USF-07-41 ≥ 65 years	
	CSL Influenza Vaccine N = 1087 - 1088 [b]	Placebo N = 266 [b]	CSL Influenza Vaccine N = 10,015 [b]	Placebo N = 5005 [b]	CSL Influenza Vaccine N = 630 [b]	Comparator N = 636 [b]
Local Adverse Reactions						
Tenderness (Pain on touching)	60	18	69	17	36	31
Pain (without touching)	40	9	48	11	15	14
Redness	16	8	4	<1	3	1
Swelling	9	1	4	<1	7	8
Bruising	5	1	1	1	<1	1
Systemic Adverse Events						
Headache	26	26	25	23	9	11
Malaise	19	19	29	26	7	6
Muscle aches	13	9	21	12	9	8
Nausea	6	9	7	6	2	1
Chills/Shivering	3	2	5	4	2	2
Fever	1	1	3	2	<1	1

[a] Proportion of subjects reporting each solicited local adverse reaction or systemic adverse event by treatment group based on the number of subjects contributing at least one data value for an individual sign/symptom (individual event denominators).

[b] N = number of subjects in the Safety Population for each treatment group. For the CSLCT-FLU-05-09 study denominators were: N=1087 for Tenderness (Pain on touching), Pain (without touching), Redness, Swelling, and N=1088 for all other parameters.

[c] Participants who received CSL Influenza Vaccine were vaccinated with either a preservative-free or preservative-containing (thiomersal) presentation. The preservative-containing presentation is not marketed in Australia.

In Study CSLCT-FLU-05-09, headache was the only unsolicited adverse event that occurred in ≥ 5% of participants who received CSL Influenza Vaccine or placebo (8% versus 6%, respectively). In Study CSLCT-USF-06-28, unsolicited adverse events that occurred in ≥ 5% of participants who received CSL Influenza Vaccine or placebo included headache (CSL Influenza Vaccine, 12% placebo, 11%,) and oropharyngeal pain (CSL Influenza Vaccine 5%, placebo 5%). In Study CSLCT-USF-07-41, headache (5%), was the only unsolicited adverse event that occurred in ≥ 5% of participants who received CSL Influenza Vaccine .

Post-marketing surveillance:

The following adverse events have been spontaneously reported during post-approval use of Fluvax® vaccine and are in addition to the events observed during clinical trials. The adverse events reported are presented below according to System Organ Class.

Blood and Lymphatic System Disorders
Thrombocytopenia.

Immune System Disorders
Allergic or immediate hypersensitivity reactions including anaphylactic shock.

Nervous System Disorders
Neuralgia, paraesthesia and convulsions (including febrile convulsions), encephalopathy, encephalomyelitis, neuritis or neuropathy, transverse myelitis and Guillain-Barré syndrome.

Vascular Disorders
Vasculitis which may be associated with transient renal involvement.

Skin and Subcutaneous Tissue Disorders
Pruritus, urticaria and rash.

General Disorders and Administration Site Conditions
Cellulitis and large injection site swelling.
Influenza like illness

Dosage and Administration

Immunisation should be undertaken in anticipation of seasonal outbreaks of influenza.

To provide continuing protection, annual vaccination with vaccine containing the most recent strains is necessary.

Dosage:

See Indications and Precautions.

Adults and children from 5 years: 0.5 mL

One dose is sufficient for persons previously exposed to viruses of similar antigenic composition to the strain(s) present in the vaccine. For children aged 5 to under 9 years who have not previously been vaccinated, a second dose should be given after an interval of at least four weeks.

Administration:

Shake before use. After shaking, the vaccine should appear as a homogenous suspension. The vaccine must be inspected visually prior to administration and should not be used if there is any variation of physical appearance.
See Description.

The vaccine should be administered by intramuscular or deep subcutaneous injection.

Fluvax® vaccine is presented as a single-use syringe and any remaining contents should be discarded.

Fluvax® vaccine can be administered concurrently with other vaccines, however separate syringes and a separate arm should be used.

Overdosage

There is no specific information on overdose of CSL Influenza Vaccine.
For general advice on overdose management:
In Australia, contact the Poisons Information Centre on 131 126.
In New Zealand, call the New Zealand Poisons Centre on 0800 POISON or 0800 764 766.

Presentation and Storage Conditions

Presentation:

Each disposable syringe contains a single 0.5 mL dose of vaccine.

The Fluvax® vaccine syringe (with fixed-needle) is supplied encased within a clear film wrapper or blister pack. The presence of the film wrapper/blister pack provides assurance that the product has not been opened. Do not use if the film wrapper or blister pack (seal or backing) is damaged or missing.

A Fluvax® vaccine needle-free syringe supplied in a blister pack is also registered but is currently not marketed.

Storage Conditions:

Fluvax® vaccine should be stored, protected from light, at 2ºC to 8ºC. IT MUST NOT BE FROZEN.

Medicine Classification

Prescription Medicine.

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