

NEW ZEALAND DATA SHEET

FLUARIX®

Inactivated split influenza vaccine

FLUARIX is an inactivated and purified split influenza vaccine, prepared in embryonated eggs.

The antigen composition and strains for the approaching influenza season are determined by the World Health Organisation (WHO). This corresponds to the following types and subtypes for the 2016 season:

A/California/7/2009 (H1N1) - like virus
A/Hong Kong/4801/2014 (H3N2) - like virus
B/Brisbane/60/2008 - like virus

Presentation

Each 0.5 mL vaccine dose contains 15 mcg haemagglutinin of each of the recommended strains (total of 45 mcg haemagglutinin). The vaccine preparation also contains alpha tocopheryl acid succinate, sodium chloride, magnesium chloride, potassium chloride, potassium phosphate monobasic, sodium phosphate dibasic dodecahydrate, polysorbate 80, and octoxinol 10 in water for injections. Residual amounts of ovalbumin ≤ 0.05 mcg and formaldehyde ≤ 5 mcg, but also traces of gentamicin sulfate, hydrocortisone, and sodium deoxycholate from the manufacturing process may be present.

Fluarix meets the WHO requirements for biological substances and influenza vaccines.

Indications

Fluarix is indicated for prophylaxis against influenza in adults and children older than six months of age. Because of the possibility of increased morbidity and mortality from complications of influenza, vaccination is especially recommended for the following:

- Persons over 60 years of age,
- Persons who suffer from diseases of the cardiovascular system, metabolic diseases (diabetes), cystic fibrosis, chronic respiratory diseases, and chronic renal insufficiency, and
- Persons with congenital or acquired immune deficiency.

Vaccination can be recommended for individuals exposed to increased risk of infection because of their occupation, such as medical personnel. In addition, prevention of disease in the workforce could lead to substantial economic benefits.

Fluarix should be administered before the beginning of the influenza season or as required by the epidemiological situations. Vaccination should be repeated every year with an age-appropriate dose of vaccine of updated antigen composition.

Dosage and Administration

Dosage

The following dosage schedule is recommended.

<i>Age</i>	<i>Dose</i>	<i>Number of doses</i>
6-35 months	0.25 mL	1 or 2 [*]
3-8 years	0.5 mL	1 or 2 [*]
>9 years	0.5 mL	1

^{*}Two doses separated by at least four weeks if the vaccine is being administered for the first time.

Method of administration

FLUARIX can be administered intramuscularly or subcutaneously.

FLUARIX should be administered subcutaneously to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

FLUARIX should under no circumstances be administered intravenously.

Contraindications

FLUARIX should not be administered to subjects with known hypersensitivity to egg proteins, to gentamicin or to any other constituent of the vaccine.

Warnings and Precautions

As with other vaccines, the administration of FLUARIX should be postponed in subjects suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in deferral of vaccination.

FLUARIX will only prevent disease caused by influenza viruses.

Infections with other agents causing flu-like symptoms are not prevented by the vaccine.

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

FLUARIX should under no circumstances be administered intravenously.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Use in pregnancy

Adequate human data on use during pregnancy are not available. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive and developmental

toxicity. However, as with all inactivated viral vaccines, the risks to the foetus are considered to be negligible. FLUARIX should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

Use in lactation

Adequate human data on use during lactation and adequate animal reproduction studies are not available. There is no known contraindication in the use of FLUARIX during lactation.

Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

Latex

Prefilled syringe with attached needle

This presentation of Fluarix cannot be considered latex-free. The removable needle shield contains natural rubber latex.

Prefilled syringe with separate needle

The syringe cap, syringe plunger and needle protector of the prefilled syringes of Fluarix with separate needles are not made with natural rubber latex.

Adverse Effects

Clinical trial data

In controlled clinical studies, Fluarix was administered to more than 23,700 subjects aged 18 to over 60 years and to more than 8,600 subjects from 6 months to 18 years of age. Signs and symptoms were solicited in all subjects for a maximum of seven days following the administration of the vaccine. A checklist was used for this purpose. The vaccinees were also requested to report any clinical events occurring during the 28 days study period.

Undesirable effects reported are listed according to the following frequency:

Very common: $\geq 1/10$

Common: $\geq 1/100$ to $< 1/10$

Uncommon: $\geq 1/1,000$ to $< 1/100$

Rare: $\geq 1/10,000$ to $< 1/1,000$

Very rare: $< 1/10,000$

Metabolism and nutrition disorders

Very common: appetite loss¹

Psychiatric disorders

Very common: irritability¹

Nervous system disorders

Very common: drowsiness¹, headache

Uncommon: dizziness

Gastrointestinal disorders

Common: gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain)

Skin and subcutaneous tissue disorders

Common: sweating

Musculoskeletal and connective tissue disorders

Very common: myalgia

Common: arthralgia

General disorders and administration site conditions

Very common: pain at the injection site, fatigue

Common: redness², swelling² and induration at the injection site, shivering

Uncommon: fever³, ecchymosis

¹reported in subjects 6 months to < 6 years old

²very common in subjects 6 months to < 18 years of age

³common in subjects 6 months to < 18 years of age

Post marketing data

Blood and lymphatic system disorders

Rare: transient lymphadenopathy, transient thrombocytopenia

Immune system disorders

Rare: allergic reactions (including anaphylactic reactions)

Nervous system disorders

Rare: neuritis, acute disseminated encephalomyelitis, neuralgia, paraesthesia, febrile convulsions, rigours, Guillan Barré syndrome*

*Spontaneous reports of Guillain-Barré syndrome have been received following vaccination with Fluarix; however, a causal association between vaccination and Guillain-Barré syndrome has not been established.

Skin and subcutaneous tissue disorders

Rare: urticaria, pruritus, erythema, rash, angioedema

Vascular disorders:

Vasculitis associated in very rare cases with transient renal involvement

General disorders and administration site conditions

Rare: influenza-like illness, malaise

Interactions

Immunisation can be affected by concomitant immunosuppressive therapy or an existing immunodeficiency.

FLUARIX can be administered simultaneously with other vaccines. If Fluarix is to be given at the same time as another injectable vaccine, the vaccines should be administered at different injection sites.

False positive ELISA serologic tests for HIV-1, Hepatitis C, and especially HTLV-1 may occur following influenza vaccination. These transient false-positive results may be due to

cross-reactive IgM elicited by the vaccine. For this reason, a definitive diagnosis of HIV-1, Hepatitis C, or HTLV-1 infection requires a positive result from a virus-specific confirmatory test (e.g., Western Blot or immunoblot).

Overdosage

Insufficient data are available.

Further Information

Pharmacodynamic properties

FLUARIX induces humoral antibodies against the haemagglutinins. These antibodies neutralise influenza viruses.

A haemagglutinin inhibition titre equal to or greater than 1:40 in the serum is considered to be protective.

FLUARIX provides protection for the ongoing influenza season.

Pharmacodynamic effects

The seroconversion rates of FLUARIX have been assessed for each influenza vaccine season. The seroprotection rates following vaccination were in excess of the requirements from the European Committee for Medicinal Products for Human Use (CHMP) criteria for influenza vaccines (>70% for adults 18-60 years and >60% for adults 60 years and above).

Significant increases in serum titres of antibodies cross-reacting with Influenza A and B drift variants have been observed after vaccine with FLUARIX.

A clinical study performed in more than 7,600 subjects in the Czech Republic and Finland evaluated the efficacy of Fluarix to prevent culture-confirmed influenza A and/or B cases for vaccine antigenically matched strains.

Subjects were monitored for influenza-like illnesses followed by culture-confirmed influenza (see below table for results). Influenza-like illness was defined as at least one general symptom (fever $\geq 37.8^{\circ}\text{C}$ and/or myalgia) and at least one respiratory symptom (cough and/or sore throat).

Table: Attack rates and Vaccine Efficacy against Illness associated with evidence of influenza A or B Infection in adults 18 to 64 years of age (Total Vaccinated Cohort)

			Attack Rates (n/N) ¹	Vaccine Efficacy (95% CI ²)		
	N	n	%	%	LL ³	UL
Antigenically matched, culture-confirmed Influenza ⁴						
Fluarix	5,103	49	1.0	66.9	51.9	77.4
Placebo	2,549	74	2.9	-	-	-
All culture-confirmed Influenza (Matched, Unmatched and Untyped) ⁵						
Fluarix	5,103	63	1.2	61.6	46.0	72.8
Placebo	2,549	82	3.2	-	-	-

1. n/N: number of case/total number of subjects

2. CI: Confidence Interval

3. LL: Lower Limit

4. There were no vaccine matched culture-confirmed cases of A/New Caledonia/20/1999 (H1N1) or B/Malaysia/2506/2004 influenza strains with Fluarix or placebo

5. Of the 22 additional cases, 18 were unmatched and 4 were untyped; 15 of the 22 cases were A (H3N2) (11 cases with Fluarix and 4 cases with placebo).

Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of acute toxicity, local tolerance, repeated dose toxicity, reproductive/developmental toxicity, and safety pharmacology.

Pharmaceutical Precautions

Instructions for use/handling

Instructions for administration of 0.5 mL of the vaccine for use in adults and children 3 years and over

Vaccines should be inspected visually for any foreign particulate matter and/or variation of physical aspects prior to administration. Before use, the vaccine should be well shaken to obtain a colourless to slight opalescent liquid. Discard if the content appears otherwise.

When a dose of 0.5 mL is indicated, the entire content of the syringe should be injected.

Instructions for administration of 0.25 mL of the vaccine for use in children from 6 months to 35 months

When a dose of 0.25 mL is indicated, the pre-filled syringe should be held in an upright position and half of the volume should be eliminated until the stopper reaches the marking line printed on the syringe. The remaining volume of 0.25 mL should be injected.

Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibilities

FLUARIX should not be mixed with other vaccines in the same syringe.

Shelf life

The expiry date of the vaccine is indicated on the label and packaging.

When stored under the prescribed conditions, the shelf life is 12 months.

Special precautions for storage

Fluarix must be stored between 2°C and 8°C.

DO NOT FREEZE. Discard if vaccine has been frozen.

Package Quantities

Prefilled syringes supplied with or without an attached needle: 0.5 mL in packs of 1 and 10*.

* Not all presentations may be distributed in New Zealand.

Medicine Classification

Prescription Medicine.

Sponsor Details

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Date of Preparation

24 May 2016

Version: 12

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