

**FLUARIX<sup>®</sup> PRODUCT INFORMATION**  
**(Inactivated Split Influenza Vaccine)**

**DESCRIPTION**

Fluarix is an inactivated and purified split influenza vaccine. The antigen composition and strains for the 2011 influenza season corresponds to the following types:

A/California/7/2009 (H1N1) derived strain used NYMC X-181: 15µg haemagglutinin per dose.

A/Perth/16/2009 (H3N2) like strain used NYMC X-187 derived from A/Victoria/210/2009: 15µg haemagglutinin per dose.

B/Brisbane/60/2008: 15µg haemagglutinin per dose.

Fluarix is prepared using whole virus cultivated in embryonated hens' eggs. The virus is concentrated and purified by clarification, adsorption and centrifugation. The purified whole virus is then treated with the detergent sodium deoxycholate and again centrifuged, and the resulting antigen suspension is inactivated with formaldehyde.

Each 0.5 ml vaccine dose contains 15 µg haemagglutinin of each of the recommended strains. The vaccine preparation also contains alpha tocopheryl acid succinate, sodium deoxycholate, sodium chloride, magnesium chloride, potassium chloride, potassium phosphate monobasic, sodium phosphate dibasic dodecahydrate, sucrose, polysorbate 80, octoxinol 10, formaldehyde and gentamicin sulfate in water for injections.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

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

The type and amount of viral antigens in Fluarix conform to the annual requirements of the Australian Influenza Vaccine Committee (AIVC) and the New Zealand Ministry of Health.

**CLINICAL PHARMACOLOGY**

Fluarix induces humoral antibodies against haemagglutinins, the surface antigens of the virus. These antibodies neutralise influenza viruses and are important in the prevention of infection.

In clinical studies conducted with various formulations of Fluarix during 1992-2001 in adults aged 18-60 years (n= 1587), the protection rates (percentage of subjects with haemagglutinin inhibition titres >40) ranged from 76-100% (H<sub>1</sub>N<sub>1</sub> strains), 67-100% (H<sub>3</sub>N<sub>2</sub> strains) and 95-100% (B strain). In healthy subjects aged > 60 years (n=629), the protection rates against the H<sub>1</sub>N<sub>1</sub>, H<sub>3</sub>N<sub>2</sub> and B strains ranged from 72-100%, 69-96% and 92-100% respectively.

Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccinal immunity varies but is usually 6-12 months.

Protection afforded as a result of vaccination with Fluarix is specific to the influenza strains contained in Fluarix or to closely related strains.

## **INDICATIONS**

Fluarix is indicated for the prevention of influenza caused by influenza virus types A and B.

The NHMRC currently recommends annual vaccination against influenza for the following groups:

All adults aged 65 years and over.

All Aboriginal and Torres Strait Islander people aged 15 years and over.

Adults and children ( $\geq$  6 months old) with conditions predisposing to severe influenza

- Cardiac disease including cyanotic congenital heart disease, coronary artery disease and congestive heart disease
- Chronic respiratory conditions including
  - suppurative lung disease, bronchiectasis, cystic fibrosis
  - chronic obstructive pulmonary disease and chronic emphysema.
  - Severe asthma defined as requiring frequent hospital visits
- Other chronic illnesses requiring regular medical follow-up or hospitalisation including
  - diabetes mellitus,

- chronic metabolic diseases,
- chronic renal failure,
- haemoglobinopathies
- impaired immunity (including drug-induced immune impairment).
- Chronic neurological conditions (eg. multiple sclerosis, spinal cord injuries, seizure disorders or other neuromuscular disorders) that can compromise respiratory function or expulsion of respiratory secretions or that can increase the risk for aspiration.
- People with impaired immunity including HIV.
- Long-term aspirin use in children, aged 6 months to 10 years.
- Pregnant women. It is recommended that influenza vaccine be offered in advance to women planning a pregnancy, and to women who will be in the second or third trimester of pregnancy during the influenza season, including those in the first trimester at the time of vaccinations.
- Residents of nursing homes and other long term care facilities.
- Homeless people and those providing care to them

People who may potentially transmit influenza to those at high risk of complications from influenza.

- staff of nursing homes
- Health care providers, and
- Staff of long-term care facilities,
- Household contacts (including children  $\geq$  6 months old) of individuals in high-risk groups.

People involved in the commercial poultry industry or in culling poultry during confirmed avian influenza activity

People providing essential services

Workers in other industries if judged to be cost-saving.

Travellers (including any person who wishes to reduce the chance of becoming infected with influenza, and those at increased risk. Persons vaccinated with the previous season's vaccine before travel should be revaccinated in the autumn with the current vaccine.

## **CONTRAINDICATIONS**

Fluarix should not be administered to subjects with known hypersensitivity to egg proteins (eggs, chicken feathers), gentamicin or any other excipient of the vaccine.

As with other vaccines, the administration of Fluarix should be postponed in subjects suffering from acute severe febrile illness (fever > 38.5°C). The presence of a minor illness with or without fever should not contraindicate the use of Fluarix.

## **WARNINGS AND PRECAUTIONS**

**Fluarix should under no circumstances be administered intravenously.**

As with all injectable vaccines, appropriate medical treatment (ie adrenaline) should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

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

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

Patients with a history of Guillain-Barre Syndrome (GBS) with an onset within six weeks of an influenza vaccination may be at increased risk of again developing GBS if given influenza vaccine. Such risk should be weighed against the benefits to the individual patient of influenza vaccination.

As patients with a history of GBS have an increased likelihood of again developing the syndrome, the chance of them coincidentally developing the syndrome following influenza vaccination may be higher than in individuals with no history of GBS.

Fluarix will only prevent disease caused by influenza viruses of the types specified. Infections with other agents causing flu-like symptoms are not prevented by the vaccine.

### **Use in Pregnancy (Category B2)**

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. Although there is no convincing evidence of risk to the

foetus from immunisation of pregnant women using inactivated viral vaccines, Fluarix should be used during pregnancy only when clearly needed.

The NHMRC states that influenza vaccine is safe for pregnant women. There is evidence from a number of studies that pregnant women, particularly during the second and third trimester, are at increased risk of influenza-associated complications. The NHMRC therefore recommends that all women who will be in the second or third trimester of pregnancy during the influenza season be vaccinated in advance, so that they will be protected during that period.

### **Use in Lactation**

Adequate human data on use during lactation and adequate animal reproduction studies are not available. There is no known contra-indication in the use of Fluarix during lactation.

### **Interactions**

Fluarix can be administered simultaneously with other vaccines, however separate syringes and separate injection sites should be used.

Influenza vaccine can impair the metabolism of warfarin, theophylline, phenytoin, phenobarbitone and carbamazepine by the hepatic cytochrome P450 system. Results from studies have been variable in degree of interaction and time after vaccination for the interaction to take effect. The interaction may be variable from individual to individual. Patients taking warfarin, theophylline, phenytoin, phenobarbitone or carbamazepine should be advised of the possibility of an interaction and told to look out for signs of elevated levels of their medication.

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

### **Effect on Laboratory tests**

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).

## **ADVERSE REACTIONS**

### **Clinical Trial Data**

Fluarix is well tolerated.

In controlled clinical studies, Fluarix was administered to more than 22,000 participants aged 18 to over 60 years and to more than 2,000 participants from 6 months to 18 years of age. Signs and symptoms were solicited in all participants for four 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 21 day 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  $< 1/1,000$ )

### **Metabolism and nutrition disorders**

Very common: appetite loss<sup>1</sup>

### **Psychiatric disorders**

Very common: irritability<sup>1</sup>

### **Nervous system disorders**

Very common: drowsiness<sup>1</sup>, headache

Uncommon: dizziness

### **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: redness<sup>2</sup>, swelling<sup>2</sup> and induration at the injection site, shivering

Uncommon: fever<sup>3</sup>, ecchymoses

<sup>1</sup>reported in subjects 6 months to 5 years old

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

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

### **Post-Marketing Surveillance**

Neurological disorders may have a temporal association with influenza vaccination, but no causal relationship has been established. An association between the A/New Jersey/76 swine influenza and Guillain-Barre Syndrome (GBS) has been demonstrated. More recently, an association between GBS and the influenza vaccines used in the Northern Hemisphere in the 1992-3 and 1993-4 seasons has been reported. Even with an estimated excess risk of 1 to 2 GBS cases per million persons vaccinated, this risk is still substantially smaller than the risk of severe influenza illness and its complications.

#### **Blood and lymphatic system disorders**

Rare: transient lymphadenopathy

#### **Immune system disorders**

Rare: allergic reactions (including anaphylactic reactions)

#### **Nervous system disorders**

Rare: neuritis, acute disseminated encephalomyelitis

#### **Gastrointestinal disorders**

Rare: vomiting

#### **Skin and subcutaneous tissue disorders**

Rare: urticaria, pruritus, erythema, rash, angioedema

#### **General disorders and administration site conditions**

Rare: influenza-like illness, malaise

## **DOSAGE AND ADMINISTRATION**

### **DOSAGE**

One dose is sufficient for persons previously exposed to viruses of similar antigenic composition to the strain(s) present in the vaccine. Children aged under 9 years who are receiving the influenza vaccine for the first time, are recommended two doses of vaccine separated by an interval of at least 4 weeks. The vaccine should be administered by deep subcutaneous injection.

Adults and children over 3 years: 0.5mL

Children, 6 months to 3 years: 0.25mL

Note: Influenza vaccine should be administered to children under 5 years of age with care and preferably only if they have a chronic debilitating disease, especially those with chronic cardiac, pulmonary, renal and metabolic disorders.

## ADMINISTRATION

Fluarix can be administered intramuscularly or subcutaneously. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

In patients with thrombocytopenia or bleeding disorders the vaccine should be administered subcutaneously.

## INSTRUCTIONS FOR USE

For a 0.5mL dose, the entire volume should be injected.

A marking line on the pre-filled syringe indicates a volume of 0.25mL.

For a 0.25mL dose, the pre-filled syringe should be held in an upright position and the excess volume expelled until the leading edge of the stopper reaches the marking line printed on the syringe. The volume remaining in the syringe should be injected.

## VACCINATION SCHEDULE

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.

Fluarix is for single use only. Discard any remaining contents.

## **STORAGE**

Fluarix must be stored between +2°C and +8°C and be protected from light.

DO NOT FREEZE. Discard if vaccine has been frozen.

The expiry date of the vaccine is indicated on the label and packaging. The shelf life of Fluarix is 12 months from the date of manufacture if stored between temperatures of +2°C and +8°C.

## **PRESENTATIONS**

Fluarix is colourless to slightly opalescent and is presented in prefilled syringes.

The prefilled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia requirements.

**MANUFACTURER**

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