Fluarix™

461452

Fluarix™
Fluarix™ Junior
Influenza vaccine (split virion, inactivated)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluarix™ is an inactivated influenza vaccine (split virion), containing antigens (propagated in embryonated eggs) equivalent to the following types and subtypes:
A/California/7/2009 (H1N1)pdm09-like strain [variant A/Christchurch/16/2010 (NIB-74xp)]
A/Victoria/361/2011 (H3N2)-like strain [variant A/Texas/50/2012 (NYMC X-223A)]
B/Massachusetts/02/2012-like strain [variant B/Massachusetts/02/2012 (NYMC BX-51B)]
This vaccine complies with the WHO recommended strains (Northern Hemisphere) for the season 2013/2014.
Each 0.5 ml vaccine dose (Fluarix™) contains 15 µg haemagglutinin of each of the recommended strains.
Each 0.25 ml vaccine dose (Fluarix™ Junior) contains 7.5 µg haemagglutinin of each of the recommended strains.
Fluarix™ meets the WHO requirements for biological substances and influenza vaccines and the European Pharmacopoeia requirements for influenza vaccines.

PHARMACEUTICAL FORM

Suspension for injection.

CLINICAL PARTICULARS

Indications

Fluarix™ is recommended for prophylaxis against influenza in adults and children older than 6 months of age.

Dosage and Administration

Adults and children over 3 years of age: one dose of 0.5 ml.
Children from 6 to 36 months of age: one dose of 0.25 ml or 0.5 ml*.
Children less than 9 years who have not previously been vaccinated should receive a second administration of the same dosage (i.e. 0.25 ml or 0.5 ml*) after an interval of at least 4 weeks.
Fluarix™ should be administered before the beginning of the influenza season or as required by the epidemiological situation. Vaccination should be repeated every year with an age-appropriate dose of vaccine of updated antigen composition.
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.
* Fluarix™ should be used in accordance with available official recommendations.

Contraindications

Fluarix™ should not be administered to subjects with known hypersensitivity to the active substances, to any of the excipients, to egg, to chicken protein, formaldehyde, gentamicin sulphate or sodium deoxycholate.

Warnings and Precautions

As with other vaccines, the administration of Fluarix™ should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor illness with or without fever should not contraindicate the use of Fluarix™.
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 an anaphylactic event following the administration of the vaccine.
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.

Interactions

Immunisation can be affected by concomitant immunosuppressive therapy or an existing immunodeficiency.
Fluarix™ can be administered simultaneously with other vaccines. However, different injection sites must be selected.
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.

Pregnancy and Lactation

The safety of Fluarix™ when administered to pregnant women has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive and developmental toxicity (see "*Non-clinical information*"). Fluarix™ should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.
The safety of Fluarix™ when administered to breastfeeding women has not been evaluated.

Effects on Ability to Drive and Use Machines

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

Adverse Reactions

Clinical trials

In controlled clinical studies, Fluarix™ was administered to more than 22,000 subjects aged 18 to over 60 years and to more than 2,000 subjects from 6 months to 18 years of age. Signs and symptoms were solicited in all subjects for 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 30 days study period.
Adverse reactions reported are listed according to the following frequency:

Very common:	≥ 1/10
Common:	≥1/100 to <1/10
Uncommon:	≥1/1,000 to <1/100
Rare:	≥1/10,000 to <1/1,000
Very rare:	<1/10,000

Very common: pain at the injection site, appetite loss[1], irritability[1], drowsiness[1], headache, fatigue, myalgia
Common: redness[2], swelling[2] and induration at the injection site, sweating, shivering, arthralgia
Uncommon: dizziness, fever[3]
[1]reported in subjects 6 months to 5 years old
[2]very common in subjects 6 months to 18 years of age
[3]common in subjects 6 months to 18 years of age

Post-marketing surveillance

Rare: transient lymphadenopathy, allergic reactions (including anaphylactic reactions), neuritis, acute disseminated encephalomyelitis, Guillain-Barré syndrome*, vomiting, urticaria, pruritus, erythema, rash, angioedema, influenza-like illness, malaise
* 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.

Overdose

Not applicable.

PHARMACOLOGICAL PROPERTIES Pharmacodynamics

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. Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccination immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6 - 12 months.
Fluarix™ provides protection for the ongoing influenza season. The seroconversion rates have been assessed for the influenza vaccine season 2012-2013, containing the A/California/7/2009 (H1N1)pdm09-like strain [variant A/Christchurch/16/2010 (NIB-74xp)], A/Victoria/361/2011 (H3N2)-like strain [variant A/Victoria/361/2011 (IVR-165)], B/Wisconsin/1/2010-like strain [variant B/Hubei-Wujiagang/158/2009 (NYMC BX-39)]. The protection rates following vaccination were in excess of the requirements of the European Committee for Medicinal Products for Human Use (CHMP) criteria for influenza vaccines (> 70% for adults 18 - 60 years and

> 60% for adults above 60 years).
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 ≥37.8°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).

Pharmacokinetics

Not relevant for vaccines.

Clinical Studies

See section *Pharmacodynamics*.

Pre-clinical 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 PARTICULARS

List of Excipients

Sodium chloride, disodium phosphate dodecahydrate, potassium dihydrogen phosphate, potassium chloride, magnesium chloride hexahydrate, α-tocopheryl hydrogen succinate, polysorbate 80, octoxinol 10 and water for injections.

Incompatibilities

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

Shelf Life

The expiry date is indicated on the label and packaging.

Special Precautions for Storage

Store at +2°C to +8°C (in a refrigerator).
Do not freeze.
Store in the original packaging in order to protect from light.

Nature and Contents of Container

Fluarix™ is colourless to slightly opalescent and is presented in ampoules, prefilled syringes or vials.
The ampoules, syringes and vials are made of neutral glass type I, that conform to European Pharmacopoeia requirements.

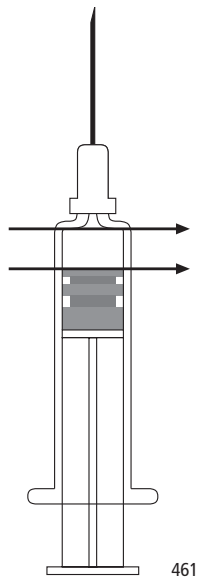
Instructions for Use/Handling

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 slightly opalescent liquid. Discard if the content appears otherwise. Any unused product or waste material should be disposed of in accordance with local requirements.

Administration of a 0.25 ml dose of Fluarix™

If a 0.25 ml dose (Fluarix™ Junior) is not available, 0.25 ml dose of Fluarix™ can be administered using the 0.5 ml prefilled syringe, it is recommended that 0.25 ml of vaccine is eliminated from the syringe before administration to the vaccinee.
For syringes with a line marked at 0.25 ml
Hold the prefilled syringe in an upright position and then push the plunger until the stopper reaches the line marked on the syringe that corresponds to 0.25 ml. The 0.25 ml dose of vaccine remaining in the syringe should then be administered to the vaccinee.
For syringes without a line marked at 0.25 ml
For syringes without a line corresponding to 0.25 ml, the picture at the end of this leaflet can be used to measure a 0.25 ml dose of Fluarix™. Align the syringe with the picture so that the upper edge of the syringe corresponds to the upper arrow. Push the plunger until the stopper reaches the lower arrow. The 0.25 ml dose of vaccine remaining in the syringe should then be administered to the vaccinee.
Not all presentations are available in every country.

Fluarix is a trademark of the GlaxoSmithKline group of companies.



461452

Version number: GDS08/IPI22 (NH) / Date of issue: April 2013

Manufacturer:
GlaxoSmithKline Biologicals, Branch of SmithKline Beecham Pharma GmbH & Co. KG, Dresden, Germany
Tel: (49) 351 45610 Fax: (49) 351 4561211