Fluarix™ NH

1. NAME OF MEDICINAL PRODUCT
Fluarix™ NH
Influenza vaccine (split virion, inactivated)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Fluarix™ NH 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)-like strain [variant A/California/7/2009 (NYMC X-181)]
A/Perth/16/2009 (H3N2)-like strain [variant A/Victoria/210/2009 (NYMC X-187)]
B/Brisbane/60/2008
This vaccine complies with the WHO recommended strains (Northern Hemisphere) for the season 2011/2012.
Each 0.5 ml vaccine dose (Fluarix™ NH) contains 15 μg haemagglutinin of each of the recommended strains.
Each 0.25 ml vaccine dose (Fluarix™ NH Junior) contains 7.5 μg haemagglutinin of each of the recommended strains.
Fluarix™ NH meets the WHO requirements for biological substances and influenza vaccines and the European Pharmacopoeia requirements for influenza vaccines.

3. PHARMACEUTICAL FORM
Suspension for injection.

4. CLINICAL PARTICULARS
4.1 Therapeutic Indications
Fluarix™ NH is recommended for prophylaxis against influenza in adults and children older than 6 months of age.

4.2 Posology and Method of Administration
Posology
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*.
For children who have not previously been vaccinated, a second dose should be given after an interval of at least 4 weeks.
Fluarix™ NH 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.
Method of administration
Fluarix™ NH can be administered intramuscularly or subcutaneously.
Fluarix™ NH should be administered subcutaneously to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Fluarix™ NH should under no circumstances be administered intravenously.

* Fluarix™ NH should be used in accordance with available official recommendations.

4.3 Contra-indications

Fluarix™ NH 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.

4.4 Special Warnings and Special Precautions for Use

As with other vaccines, the administration of Fluarix™ NH should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor illness with or without fever should not contra-indicate the use of Fluarix™ NH.

Fluarix™ NH 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.

4.5 Interaction with Other Medicaments and Other Forms of Interaction

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

Fluarix™ NH can be administered simultaneously with other vaccines. However, different injection sites must be selected.

4.6 Pregnancy and Lactation

The safety of Fluarix™ NH 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™ NH should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the foetus.

The safety of Fluarix™ NH when administered to breastfeeding women has not been evaluated.

4.7 Effects on Ability to Drive and Use Machines

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

Clinical trials

In controlled clinical studies, Fluarix™ NH 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 loss¹, irritability¹, drowsiness¹, headache, fatigue, myalgia
Common: redness², swelling² and induration at the injection site, sweating, shivering, arthralgia
Uncommon: dizziness, fever³

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™ NH; however, a causal association between vaccination and Guillain-Barré syndrome has not been established.

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Fluarix™ NH 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.
Seroconversion 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™ NH provides protection for the ongoing influenza season.

The seroconversion rates have been assessed for the influenza vaccine season 2010-2011, containing the A/California/7/2009 (H1N1)-like strain [variant A/California/7/2009 (NYMC X-181)], A/Perth/16/2009 (H3N2)-like strain [variant A/Victoria/210/2009 (NYMC X-187)], B/Brisbane/60/2008.

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™ NH 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)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>n</th>
<th>%</th>
<th>Vaccine Efficacy (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Antigenically matched, culture-confirmed Influenza</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluarix™ NH</td>
<td>5,103</td>
<td>49</td>
<td>1.0</td>
<td>66.9, 51.9, 77.4</td>
</tr>
<tr>
<td>Placebo</td>
<td>2,549</td>
<td>74</td>
<td>2.9</td>
<td>-</td>
</tr>
<tr>
<td>All culture-confirmed Influenza (Matched, Unmatched and Untyped)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluarix™ NH</td>
<td>5,103</td>
<td>63</td>
<td>1.2</td>
<td>61.6, 46.0, 72.8</td>
</tr>
<tr>
<td>Placebo</td>
<td>2,549</td>
<td>82</td>
<td>3.2</td>
<td>-</td>
</tr>
</tbody>
</table>

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™ NH 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™ NH and 4 cases with placebo).

5.2 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.
5.3 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.

6. PHARMACEUTICAL PARTICULARS
6.1 List of Excipients
Sodium Chloride, Disodium Phosphate Dodecahydrate, Potassium Dihydrogen Phosphate, Potassium Chloride, Magnesium Chloride Hexahydrate, α-tocopheryl Hydrogen Succinate, Polysorbate 80, Octoxynol 10 and Water for Injections.

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

6.3 Shelf-life
The expiry date of the vaccine is indicated on the label and packaging.

6.4 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.

6.5 Nature and Content of Container
Fluarix™ NH 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.

6.6 Instructions for Use and Handling and Disposal
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™ NH
If a 0.25 ml dose (Fluarix™ NH Junior) is not available, 0.25 ml dose of Fluarix™ NH 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™ NH. 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.

7. MARKETING AUTHORISATION HOLDER
GlaxoSmithKline (Thailand) Ltd.

8. MARKETING AUTHORISATION NUMBER
2C 21/45 (N)

9. DATE OF FIRST AUTHORISATION
26 December 2002 (unconditional license).

Fluarix is a trademark of the GlaxoSmithKline group of companies.

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