ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Prepandrix suspension and emulsion for emulsion for injection.
Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After mixing, 1 dose (0.5 ml) contains:

Split influenza virus inactivated, containing antigen* equivalent to:

A/VietNam/1194/2004 (H5N1) like strain used (NIBRG-14)	3.75 micrograms**

* propagated in eggs
** haemagglutinin

AS03 adjuvant composed of squalene (10.68 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.85 milligrams)

The suspension and emulsion vials once mixed form a multidose container. See section 6.5 for the number of doses per vial.

Excipients: It contains 5 micrograms thiomersal

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Suspension and emulsion for emulsion for injection.
The suspension is a colourless light opalescent liquid.
The emulsion is a whitish homogeneous liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Active immunisation against H5N1 subtype of Influenza A virus.
This indication is based on immunogenicity data from healthy subjects aged 18-60 years following administration of two doses of vaccine prepared from A/VietNam/1194/2004 NIBRG-14 (H5N1) (see section 5.1).

Prepandrix should be used in accordance with official guidance.

4.2 Posology and method of administration

Posology

Adults from the age of 18 to 60 years: 1 dose of 0.5 ml at an elected date.
A second dose of vaccine should be given after an interval of at least three weeks.

There is no experience in children and adults above 60 years of age.

For further information, see section 5.1.

Method of administration

Immunisation should be carried out by intramuscular injection.

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to any of the constituents or trace residues (egg and chicken protein, ovalbumin, formaldehyde, gentamicin sulphate and sodium deoxycholate) of this vaccine. See sections 4.4, 4.8 and 6.1.

Acute severe febrile illness. Immunisation should be postponed.

4.4 Special warnings and precautions for use

Caution is needed when administrating this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients, to thiomersal and to residues ((egg and chicken protein, ovalbumin, formaldehyde, gentamicin sulphate and sodium deoxycholate).

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

Prepandrix should under no circumstances be administered intravascularly or intradermally.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

A protective immune response may not be elicited in all vaccinees (see section 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

The vaccine should not usually be given at the same time as other vaccines. However, if co-administration with another vaccine is considered to be essential, the vaccines should be injected into separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false-positive serology test results may be obtained by the ELISA method for antibody to human immunodeficiency virus-1 (HIV-1), hepatitis C virus and, especially, HTLV-1. In such cases, the Western blot method is negative. These transitory false-positive results may be due to IgM production in response to the vaccine.

4.6 Pregnancy and lactation

No data have been generated in pregnant women with Prepandrix or with any other vaccine that contains the AS03 adjuvant.

Animal studies do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryonal/foetal development, parturition or post-natal development (see section 5.3).

Healthcare providers need to assess the benefits and potential risks of administering the vaccine to pregnant women taking into consideration official recommendations.

There are no data regarding the use of Prepandrix during lactation. The potential benefits to the mother and risks to the infant should be considered before administering Prepandrix during lactation.

4.7 Effects on ability to drive and use machines

Some of the effects mentioned under section 4.8 “Undesirable Effects” may affect the ability to drive or operate machinery.

4.8 Undesirable effects

- Clinical trials

The incidence of adverse reactions has been evaluated in approximately 5,000 subjects 18 years old and above who received formulations containing at least 3.75 microgram HA/AS03.

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)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Blood and lymphatic system disorders
Common: lymphadenopathy

Nervous system disorders
Very common: headache
Uncommon: paraesthesia, somnolence, dizziness

Gastrointestinal disorders
Uncommon: gastro-intestinal symptoms (such as diarrhoea, vomiting, abdominal pain, nausea)

Skin and subcutaneous tissue disorders
Common: ecchymosis at the injection site, sweating increased
Uncommon: pruritus, rash

Musculoskeletal and connective tissue disorders
Very common: arthralgia, myalgia

General disorders and administration site conditions
Very common: induration, swelling, pain and redness at the injection site, fever, fatigue,
Common: shivering, influenza like illness, injection site reactions (such as warmth, pruritus)
Uncommon: malaise

Psychiatric disorders
Uncommon: insomnia

- Post-marketing surveillance

No post-marketing surveillance data are available following Prepandrix administration.

From Post-marketing surveillance with interpandemic trivalent vaccines, the following adverse reactions have been reported:

Uncommon:
Generalised skin reactions including urticaria

Rare:
Neuralgia, convulsions, transient thrombocytopenia.
Allergic reactions, in rare cases leading to shock, have been reported.

Very rare:
Vasculitis with transient renal involvement.
Neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome.

This medicinal product contains thiomersal (an organomercuric compound) as a preservative and therefore, it is possible that sensitisation reactions may occur (see section 4.4).

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccines, ATC Code J07BB02

Immune response against vaccine strain contained in Prepandrix:

In a consistency study, more than 900 subjects aged 18-60 years received Prepandrix following a 0, 21 days schedule.

Twenty-one days after the first and second dose of the vaccine, the seroprotection rate, the seroconversion rate and seroconversion factor for anti-haemagglutinin (anti-HA) antibody were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate*†	44.5%	94.3%
Seroconversion rate†	42.5%	93.7%
Seroconversion factor†	4.1	39.8

* anti-HA ≥1:40
† seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥1:40; seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of ≥1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre; seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

Twenty-one days after administration of the second dose, 96.0% of subjects had a 4-fold increase in serum neutralising antibody titres.

A neutralising antibody titre of at least 1:80 was achieved in 97.8% of subjects at day 42.

In a dose finding study in subjects aged 18-60 years, 50 subjects received a dose of 3.75 micrograms HA/AS03 in a volume of 1 ml at 0 and 21 days. The seroprotection rates, seroconversion rates and seroconversion factors for anti-haemagglutinin (anti-HA) antibody at day 42 (post dose 2) and day 180 (persistence) were as follows:

anti-HA antibody	Day 42	Day 180
Seroprotection rate*†	84%	54%
Seroconversion rate†	82%	52%
Seroconversion factor†	27.9	4.4

* anti-HA ≥1:40

† seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥1:40; seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of ≥1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre; seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

A 4-fold increase in serum neutralising antibody titres was observed in 85.7% of subjects at day 42 and 72% at day 180.

Cross-reactive immune response against variants of A/Vietnam/1194/2004 (H5N1):

In the consistency study the seroprotection rate, seroconversion rate and seroconversion factor for anti-haemagglutinin (anti-HA) antibody against A/Indonesia/5/2005 at 21 days after the second dose were as follows:

anti-HA antibody	A/Indonesia/5/2005 N = 924
Seroprotection rate*†	50.2%
Seroconversion rate†	50.2%
Seroconversion factor†	4.9

* anti-HA ≥1:40

† seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥1:40; seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of ≥1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre; seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

A 4-fold increase in serum neutralising antibody titres was obtained in 91.4% of subjects at day 42.

In the dose finding studythe seroprotection rate, seroconversion rate and seroconversion factor against H5N1 drift variants 21 days after the second dose were as follows:

anti-HA antibody	A/Indonesia/5/2005 N = 50	A/Anhui/01/2005 N = 20	A/Turkey/Turkey/1/2005 N = 20
Seroprotection rate*†	20.0%	35.0%	60.0%
Seroconversion rate†	20.0%	35.0%	60.0%
Seroconversion factor†	2.0	3.4	4.7

* anti-HA ≥1:40

† seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥1:40; seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of ≥1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre; seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

Twenty one days after the second dose, a 4-fold increase in serum neutralising antibody titres was obtained in 77.1% of subjects against the A/Indonesia/5/2005 strain, in 75.0% of subjects against A/Anhui/01/2005 and in 85.0% of subjects against A/Turkey/Turkey/1/2005.

Information from non-clinical studies:

The ability to induce protection against homologous and heterologous vaccine strains was assessed non-clinically using ferret challenge models.

In each experiment, four groups of six ferrets were immunized intramuscularly with an AS03 adjuvanted vaccine containing HA derived from H5N1/A/Vietnam/1194/04 (NIBRG-14). Doses of 15, 5, 1.7 or 0.6 micrograms of HA were tested in the homologous challenge experiment, and doses of 15, 7.5, 3.8 or 1.75 micrograms of HA were tested in the heterologous challenge experiment. Control

groups included ferrets immunized with adjuvant alone, non-adjuvanted vaccine (15 micrograms HA) or phosphate buffered saline solution. Ferrets were vaccinated on days 0 and 21 and challenged by the intra-tracheal route on day 49 with a lethal dose of either H5N1/A/Vietnam/1194/04 or heterologous H5N1/A/Indonesia/5/05. Of the animals receiving adjuvanted vaccine, 87% and 96% were protected against the lethal homologous or heterologous challenge, respectively. Viral shedding into the upper respiratory tract was also reduced in vaccinated animals relative to controls, suggesting a reduced risk of viral transmission. In the unadjuvanted control group, as well as in the adjuvant control group, all animals died or had to be euthanized as they were moribund, three to four days after the start of challenge.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, acute and repeated dose toxicity, local tolerance, female fertility, embryo-foetal and postnatal toxicity (up to the end of the lactation period).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Suspension vial:
Polysorbate 80
Octoxynol 10
Thiomersal
Sodium chloride (NaCl)
Disodium hydrogen phosphate (Na_2HPO_4)
Potassium dihydrogen phosphate (KH_2PO_4)
Potassium chloride (KCl)
Magnesium chloride ($MgCl_2$)
Water for injections

Emulsion vial:
Sodium chloride (NaCl)
Disodium hydrogen phosphate (Na_2HPO_4)
Potassium dihydrogen phosphate (KH_2PO_4)
Potassium chloride (KCl)
Water for injections

For adjuvants, see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

18 months.
After mixing, the vaccine should be used within 24 hours. Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

One pack containing:
- one pack of 50 vials (type I glass) of 2.5 ml suspension (10 x 0.25 ml doses) with a stopper (butyl rubber).
- two packs of 25 vials (type I glass) of 2.5 ml emulsion (10 x 0.25 ml doses) with a stopper (butyl rubber).

The volume after mixing 1 vial of suspension (2.5 ml) with 1 vial of emulsion (2.5 ml) corresponds to 10 doses of vaccine (5 ml).

6.6 Special precautions for disposal and other handling

Prepandrix consists of two containers:
Vial A: multidose vial containing the antigen (suspension),
Vial B: multidose vial containing the adjuvant (emulsion).

Prior to administration, the two components should be mixed.

Instructions for mixing and administration of the vaccine:

1. Before mixing the two components, the emulsion and suspension should be allowed to reach room temperature, shaken and inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.
2. The vaccine is mixed by withdrawing the contents of the vial containing the emulsion (Vial B) by means of a syringe and by adding it to the vial containing the suspension (Vial A).
3. After the addition of the emulsion to the suspension, the mixture should be well shaken. The mixed vaccine is a whitish emulsion. In the event of other variation being observed, discard the vaccine.
4. The volume of Prepandrix (5 ml) after mixing corresponds to 10 doses of vaccine.
5. The vial should be shaken prior to each administration.
6. Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection.
7. The needle used for withdrawal must be replaced by a needle suitable for intramuscular injection.

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

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
rue de l'Institut 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Sächsisches Serumwerk Dresden
Branch of GlaxoSmithKline Biologicals
Zirkustraße 40, D-01069 Dresden
Germany

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Biologicals S.A.
89, rue de l'Institut
B-1330 Rixensart
Belgium

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable

- **OTHER CONDITIONS**

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, as described in version V01 (dated June 2006) presented in Module 1.8.1. of the Marketing Authorisation Application, is in place and functioning before and whilst the product is on the market.

Risk Management Plan
The MAH commits to performing the studies and additional pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in version RMPv3 (dated 31 January 2008) of the Risk Management Plan (RMP) presented in Module 1.8.2. of the Marketing Authorisation Application and any subsequent updates of the RMP agreed by the CHMP.

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, the updated RMP should be submitted at the same time as the next Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted

- When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities
- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached
- At the request of the EMEA

PSURs

PSUR submission when Prepandrix is used during the influenza pandemic:

During a pandemic situation, the frequency of submission of periodic safety update reports specified in Article 24 of Regulation (EC) No 726/2004 will not be adequate for the safety monitoring of a pandemic vaccine for which high levels of exposure are expected within a short period of time. Such situation requires rapid notification of safety information that may have the greatest implications for risk-benefit balance in a pandemic. Prompt analysis of cumulative safety information, in light of extent of exposure, will be crucial for regulatory decisions and protection of the population to be vaccinated. In addition, duration a pandemic, resources needed for an in-depth evaluation of Periodic Safety Update Reports in the format as defined in Volume 9a of the Rules Governing Medicinal Product in the European Union may not be adequate for a rapid identification of a new safety issue.
In consequence, as soon as the pandemic is declared (Phase 6 of the WHO global Influenza preparedness plan) and the prepandemic vaccine is used, the MAH shall submit periodic safety update reports with periodicity and format defined as follows:

Frequency of submission

- The clock will start from the first Monday after the date of announcement of the influenza pandemic (Phase 6 of the WHO Preparedness Plan) (Day 0)
- First data-lock point is 14 days later.
- Report submission is no later than day 22 (i.e. the following Monday).
- Reporting to be fortnightly for the first 3 months of the pandemic.
- Periodicity will be reviewed by the MAH and the (Co-)Rapporteur at 3 monthly intervals.

Format

The report shall include the following Tables of aggregate data using the agreed templates:

1. Fatal and/or life-threatening reactions – for each Preferred Term (PT), including the proportion of fatal reports
2. Adverse Events of Special Interest (PTs)
3. Serious unexpected reactions (PTs)
4. All events occurring in the following age groups: 6-23 months, 2-8 years, 8-17 years, 18-60 years, >60 years
   All events occurring in pregnant women
5. All events reported by patients that have been entered into the database by data-lock point
6. A cumulative overview of all events reported during the period, stratified according to type of reporter (patient or health care professional), seriousness, expectedness, and whether spontaneous or solicited.

Presentation of data will take into consideration the following recommendations:

- Serious expected reactions will be reviewed by the MAH as part of their signal detection procedures and will only form part of the report if an issue of concern arises.
- All tables will be based on number of events (presented on PT level, sorted by System Organ Class [SOC]) and not number of cases.
- Tables 1 to 4 will be based on events reported from healthcare professionals only.
- In Tables 1 to 5, numbers will be provided for events received during the reporting period and cumulatively.
- All tables will be based on generic and not product-specific data. Product-specific data can be evaluated during signal work-up.
- No line listings are required – these can be provided in signal evaluation reports as necessary.

A short summary shall also be provided with the periodic safety update reports, in which any area of concern should be highlighted, signal work-up prioritised (if the event of multiple signals) and appropriate timelines for submission of a full signal evaluation report provided. All

signal evaluation reports should be provided, including those that were subsequently not identified as being signals.

A summary of vaccine distribution shall be included and provide details of the number of doses of vaccine distributed in:

i) EU member states for the reporting period by batch number,
ii) EU member states cumulatively and
iii) the rest of the world

Official batch release: in accordance with Article 114 Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PACK CONTAINING 1 PACK OF 50 VIALS OF SUSPENSION AND 2 PACKS OF 25 VIALS OF EMULSION

1. NAME OF THE MEDICINAL PRODUCT

Prepandrix suspension and emulsion for emulsion for injection
Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After mixing, 1 dose (0.5 ml) contains:

Split influenza virus, inactivated, containing antigen equivalent to:

A/VietNam/1194/2004 (H5N1) like strain used (NIBRG-14) 3.75 micrograms*

AS03 adjuvant composed of squalene (10.68 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.85 milligrams)

* haemagglutinin

3. LIST OF EXCIPIENTS

Polysorbate 80
Octoxynol 10
Thiomersal
Sodium chloride (NaCl)
Disodium hydrogen phosphate (Na_2HPO_4)
Potassium dihydrogen phosphate (KH_2PO_4)
Potassium chloride (KCl)
Magnesium chloride ($MgCl_2$)
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension and emulsion for emulsion for injection

50 vials: suspension
25 vials x 2: emulsion

The volume after mixing 1 vial of suspension (2.5 ml) with 1 vial of emulsion (2.5 ml) corresponds to 10 doses of vaccine (5 ml)

1 dose = 0.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use

Shake before use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Suspension and emulsion to be mixed before administration

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PACK OF 50 VIALS OF SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT

Prepandrix suspension for emulsion for injection
Prepandemic influenza vaccine (H5N1)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Split influenza virus, inactivated, containing antigen equivalent to
A/VietNam/1194/2004 (H5N1) like strain used (NIBRG-14) 3.75 micrograms*

* haemagglutinin

3. LIST OF EXCIPIENTS

Polysorbate 80
Octoxynol 10
Thiomersal
Sodium chloride (NaCl)
Disodium hydrogen phosphate (Na_2HPO_4)
Potassium dihydrogen phosphate (KH_2PO_4)
Potassium chloride (KCl)
Magnesium chloride ($MgCl_2$)
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for emulsion for injection
50 vials: suspension

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Shake before use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Suspension to be exclusively mixed with emulsion before administration

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local regulations.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PACK OF 25 VIALS OF EMULSION

1. NAME OF THE MEDICINAL PRODUCT

Emulsion for emulsion for injection for Prepandrix

2. STATEMENT OF ACTIVE SUBSTANCE(S)

AS03 adjuvant composed of squalene (10.68 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.85 milligrams)

3. LIST OF EXCIPIENTS

Sodium chloride (NaCl)
Disodium hydrogen phosphate (Na_2HPO_4)
Potassium dihydrogen phosphate (KH_2PO_4)
Potassium chloride (KCl)
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Emulsion for emulsion for injection
25 vials: emulsion

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Shake before use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Emulsion to be exclusively mixed with suspension before administration

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local regulations.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
SUSPENSION VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vial A
Prepandrix suspension for emulsion for injection
IM

2. METHOD OF ADMINISTRATION

To be mixed with Vial B before administration

3. EXPIRY DATE

EXP
After mixing: Use within 24 hours and do not store above 25°C.
Date and time of mixing:

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses (2.5 ml)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
EMULSION VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Vial B
Emulsion for emulsion for injection for Prepandrix

IM

2. METHOD OF ADMINISTRATION

To be mixed with Vial A before administration

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses (2.5 ml)

6. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Prepandrix suspension and emulsion for emulsion for injection
Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted)

Read all of this leaflet carefully before you start receiving this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for you. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT PREPANDRIX IS AND WHAT IT IS USED FOR

Prepandrix is a vaccine for use in adults from 18 to 60 years old. It is intended to be given before or during the next influenza (flu) pandemic to prevent flu caused by the H5N1 type of the virus. Pandemic flu is a type of influenza that occurs at intervals that vary from less than 10 years to many decades. It spreads rapidly around the world. The symptoms of pandemic flu are similar to those of ordinary flu but are usually more severe.

When a person is given the vaccine, the immune system (the body's natural defence system) will produce its own protection (antibodies) against the disease. None of the ingredients in the vaccine can cause flu.

As with all vaccines, Prepandrix may not fully protect all persons who are vaccinated.

2. BEFORE YOU RECEIVE PREPANDRIX

Prepandrix should not be given:

- if you have previously had a sudden life-threatening allergic reaction to any ingredient of Prepandrix (these are listed at the end of this leaflet) or to any of the substances that may be present in trace amounts as follows: egg and chicken protein, ovalbumin, formaldehyde, gentamicin sulphate (antibiotic) or sodium deoxycholate. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.

- if you have a severe infection with a high temperature (over 38°C). If this applies to you then your vaccination will be postponed until you are feeling better. A minor infection such as a cold should not be a problem, but your doctor will advise whether you can still be vaccinated with Prepandrix.

Take special care with Prepandrix:

- if you have had any allergic reaction other than a sudden life threatening allergic reaction to any ingredient contained in the vaccine, to thiomersal, to egg and chicken protein, ovalbumin

formaldehyde, gentamicin sulphate (antibiotic) or to sodium deoxycholate. (see section 6. Further information).
- if you have problems with your immune system, since your response to the vaccine may then be poor.
- if you are having a blood test to look for evidence of infection with certain viruses. In the first few weeks after vaccination with Prepandrix the results of these tests may not be correct. Tell the doctor requesting these tests that you have recently received Prepandrix.

Using other medicines or vaccines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription or have recently received any other vaccine.

There are no data on the use of Prepandrix given at the same time as other vaccines. Therefore, Prepandrix is not intended to be given at the same time as other vaccines. However, if this cannot be avoided, the other vaccine will be injected into the other arm. Any side effects that occur may be more severe.

If you take any medicines that reduce immunity to infections or have any other type of treatment (such as radiotherapy) that affects the immune system, Prepandrix can still be given but your response to the vaccine may be poor.

Pregnancy and breast-feeding
There is no information on the use of Prepandrix in pregnant or breast-feeding women. Your doctor needs to assess the benefits and potential risks of giving you the vaccine if you are pregnant or breast-feeding. Please tell your doctor if you are/may be pregnant or intend to become pregnant, or if you are breast-feeding and follow his advice.

Driving and using machines
Some effects mentioned under section 4. "Possible side effects" may affect the ability to drive or use machines.

Important information about some of the ingredients of Prepandrix
Thiomersal (preservative) is present in this product, and it is possible that you may experience an allergic reaction.

This medicinal product contains less than 1 mmol sodium (23 mg) and less than 1 mmol of potassium (39 mg) per dose, i.e. essentially sodium- and potassium-free.

3. HOW PREPANDRIX IS GIVEN

You will receive two doses of Prepandrix. The second dose should be given after an interval of at least three weeks.

The doctor or nurse will give Prepandrix as an injection into your upper arm muscle.

The vaccine should never be given into a vein or into the skin.

If you have any further questions on the use of this product, ask your doctor or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Prepandrix can cause side effects, although not everybody gets them.

♦ Very common (these may occur with 1 in 10 doses or more of the vaccine):
- Tiredness

- Headache
- Pain, redness, swelling or a hard lump at the injection site
- Fever
- Aching muscles, joint pain

♦ Common (these may occur with up to 1 in 10 doses of the vaccine):
- Warmth, itching or bruising at the injection site
- Increased sweating, shivering, flu-like symptoms
- Swollen glands in the neck, armpit or groin

♦ Uncommon (these may occur with up to 1 in 100 doses of the vaccine):
- Tingling or numbness of the hands or feet
- Dizziness
- Sleepiness
- Sleeplessness
- Diarrhoea, vomiting, stomach pain, feeling sick
- Itching, rash
- Generally feeling unwell

These reactions usually disappear within 1-2 days without treatment.

Other side effects which have occurred in the days or weeks after vaccination with ordinary flu vaccines include:

♦ Uncommon (these may occur with up to 1 in 100 doses of the vaccine):
- Generalised skin reactions including urticaria (hives)

♦ Rare (these may occur with up to 1 in 1,000 doses of the vaccine):
- Severe stabbing or throbbing pain along one or more nerves
- Fits
- Low blood platelet count which can result in bleeding or bruising
- Allergic reactions leading to a dangerous decrease of blood pressure, which, if untreated, may lead to collapse, coma and death

♦ Very rare (these may occur with up to 1 in 10,000 doses of the vaccine):
- Narrowing or blockage of blood vessels with kidney problems
- Temporary inflammation of the brain and nerves causing pain, weakness and paralysis that may spread across the body.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PREPANDRIX

Keep out of the reach and sight of children.

Before the vaccine is mixed:
Do not use the suspension and the emulsion after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

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

After the vaccine is mixed:
After mixing, use the vaccine within 24 hours and do not store above 25°C.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Prepandrix contains

- Active substance:
  After mixing, one dose (0.5 ml) contains 3.75 micrograms of haemagglutinin from the following influenza virus strain:

  A/Vietnam/1194/2004 (H5N1)

- Adjuvant:
  The emulsion vial contains an 'adjuvant' (AS03). This compound contains squalene (10.68 milligrams), DL-α-tocopherol (11.86 milligrams) and polysorbate 80 (4.85 milligrams). Adjuvants are used to improve the body's response to the vaccine.

- Other ingredients:
  The other ingredients are: polysorbate 80, octoxynol 10, thiomersal, sodium chloride (NaCl), disodium hydrogen phosphate (Na_2HPO_4), potassium dihydrogen phosphate(KH_2PO_4), potassium chloride (KCl), magnesium chloride ($MgCl_2$), water for injections

What Prepandrix looks like and contents of the pack

One pack of Prepandrix consists of:
- one pack containing 50 vials of 2.5 ml suspension (active substance) for 10 doses
- two packs containing 25 vials of 2.5 ml emulsion (adjuvant) for 10 doses

The suspension is a colourless light opalescent liquid.
The emulsion is a whitish homogeneous liquid.

Prior to administration, the two components should be mixed. The mixed vaccine is a whitish emulsion.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last approved in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency (EMEA) web site: http://www.emea.europa.eu/

The following information is intended for medical or healthcare professionals only:

Prepandrix consists of two containers:
Vial A: multidose vial containing the antigen (suspension),
Vial B: multidose vial containing the adjuvant (emulsion).

Prior to administration, the two components should be mixed.

Instructions for mixing and administration of the vaccine:

1. Before mixing the two components, the emulsion and suspension should be allowed to reach room temperature, shaken and inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.
2. The vaccine is mixed by withdrawing the contents of the vial containing the emulsion (Vial B) by means of a syringe and by adding it to the vial containing the suspension (Vial A).
3. After the addition of the emulsion to the suspension, the mixture should be well shaken. The mixed vaccine is a whitish emulsion. In the event of other variation being observed, discard the vaccine.
4. The volume of Prepandrix (5 ml) after mixing corresponds to 10 doses of vaccine.
5. The vial should be shaken prior to each administration.
6. Each vaccine dose of 0.5 ml is withdrawn into a syringe for injection.
7. The needle used for withdrawal must be replaced by a needle suitable for intramuscular injection.

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