

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

Pandemrix suspension and emulsion for emulsion for injection.  
Pandemic 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

This vaccine complies with the WHO recommendation and EU decision for the pandemic.

AS03 adjuvant composed of squalene (10.69 milligrams), DL- $\alpha$ -tocopherol (11.86 milligrams) and polysorbate 80 (4.86 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

Prophylaxis of influenza in an officially declared pandemic situation. Pandemic influenza vaccine should be used in accordance with official guidance (see sections 4.2 and 5.1).

### 4.2 Posology and method of administration

#### Posology

Persons not previously vaccinated with Prepandrix or Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals 3.75  $\mu$ g

Adults from the age of 18 years:

One dose of 0.5 ml at an elected date.

A second dose of 0.5 ml should be given after an interval of at least three weeks.

Based on very limited data, adults aged >80 years may require a double dose of Pandemrix on an elected date and again after an interval of at least three weeks in order to achieve an immune response (see section 5.1).

Persons previously vaccinated with one or two doses of Prepandrix or Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals 3.75 µg containing HA derived from a different clade of the same influenza subtype as the pandemic influenza virus:

Adults from the age of 18 years onwards: one dose of 0.5 ml at an elected date.

There is no experience in children.

For further information, see sections 4.4 and 5.1.

#### Method of administration

Immunisation should be carried out by intramuscular injection.

If a double dose is given, the injections should be given into opposite limbs.

### **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. However, in a pandemic situation, it may be appropriate to give the vaccine, provided that facilities for resuscitation are immediately available in case of need.

See section 4.4.

### **4.4 Special warnings and precautions for use**

Caution is needed when administering 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.

If the pandemic situation allows, immunisation shall be postponed in patients with severe febrile illness or acute infection.

Pandemrix should under no circumstances be administered intravascularly.

There are no data on administration of AS03-adjuvanted vaccines before or following other types of influenza vaccines intended for pre-pandemic or pandemic use.

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**

Pandemrix should not be given at the same time as other vaccines. However, if co-administration with another vaccine is indicated, immunisation should be carried out on 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 Pandemrix 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, embryonic/fetal 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.

Pandemrix may be used 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

Adverse reactions from clinical trials with the mock-up vaccine are listed here below (see section 5.1 for more information on mock-up vaccines).

Clinical studies have evaluated the incidence of adverse reactions listed below 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 ( $\geq 1/10$ )

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 ( $< 1/10,000$ )

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

##### Blood and lymphatic system disorders

Common: lymphadenopathy

##### Psychiatric disorders

Uncommon: insomnia

##### 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

- Post-marketing surveillance

No post-marketing surveillance data are available following Pandemrix 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.

This section describes the clinical experience with the mock-up vaccines.

Mock-up vaccines contain influenza antigens that are different from those in the currently circulating influenza viruses. These antigens can be considered as “novel” antigens and simulate a situation where the target population for vaccination is immunologically naïve. Data obtained with the mock-up vaccine will support a vaccination strategy that is likely to be used for the pandemic vaccine: clinical immunogenicity, safety and reactogenicity data obtained with mock-up vaccines are relevant for the pandemic vaccines.

Immune response against A/Vietnam/1194/2004 (H5N1):

In clinical studies that evaluated the immunogenicity of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 in subjects aged 18-60 years the anti-haemagglutinin (anti-HA) antibody responses were as follows:

anti-HA antibody	Immune response to A/Vietnam/1194/2004				
	0, 21 days schedule		0, 6 months schedule		
	21 days after 1 <sup>st</sup> dose N=925	21 days after 2 <sup>nd</sup> dose N=924	21 days after 1 <sup>st</sup> dose N=55	7 days after 2 <sup>nd</sup> dose N=47	21 days after 2 <sup>nd</sup> dose N=48
Seroprotection rate <sup>1</sup>	44.5%	94.3%	38.2%	89.4%	89.6%
Seroconversion rate <sup>2</sup>	42.5%	93.7%	38.2%	89.4%	89.6%
Seroconversion factor <sup>3</sup>	4.1	39.8	3.1	38.2	54.2

<sup>1</sup> seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre  $\geq 1:40$ ;

<sup>2</sup> seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of  $\geq 1:40$ , or who were seropositive at pre-vaccination and have a 4-fold increase in titre;

<sup>3</sup> seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

After two doses given 21 days or 6 months apart, 96.0% of subjects had a 4-fold increase in serum neutralising antibody titres and 98-100% had a titre of at least 1:80.

Follow up of 50 subjects aged 18-60 years who had received two doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 at 0 and 21 days showed that 84% were seroprotected (HI titre  $\geq 1:40$ ) at day 42 compared with 54% at day 180. A 4-fold increase in serum neutralising antibody titres from day 0 was observed in 85.7% at day 42 and 72% at day 180.

In another clinical study, 152 subjects aged > 60 years (stratified in ranges from 61 to 70, 71 to 80 and > 80 years of age) received either a single or a double dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 (H5N1) at 0 and 21 days. At day 42, the anti-HA antibody responses were as follows:

anti-HA antibody	Immune response to A/Vietnam/1194/2004 (D42)					
	61 to 70 years		71 to 80 years		>80 years	
	Single dose N=91	Double dose N=92	Single dose N=48	Double dose N=43	Single dose N=13	Double dose N=10
Seroprotection rate <sup>1</sup>	84.6%	97.8%	87.5%	93.0%	61.5%	90.0%
Seroconversion rate <sup>2</sup>	74.7%	90.2%	77.1%	93.0%	38.5%	50.0%
Seroconversion factor <sup>3</sup>	11.8	26.5	13.7	22.4	3.8	7.7

<sup>1</sup> seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre  $\geq 1:40$ ;

<sup>2</sup> seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of  $\geq 1:40$ , or who were seropositive at pre-vaccination and have a 4-fold increase in titre;

<sup>3</sup>seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

Although an adequate immune response was achieved at day 42 following two administrations of a single dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 (H5N1), a higher response was observed following two administrations of a double dose of vaccine.

Very limited data in seronegative subjects >80 years of age (N=5) showed that no subject achieved seroprotection rate following two administrations of a single dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 (H5N1). However, following two administrations of a double dose of vaccine, the seroprotection rate at day 42 was 75%.

The day 180 seroprotection rates in subjects aged >60 years were 52.9% for those who had received two single doses and 69.5% for those who had received two double doses at day 0 and day 21.

In addition, 44.8% and 56.1% of subjects in respective dose groups had a 4-fold increase in serum neutralising antibody titres from day 0 to day 42 and 96.6% and 100% of subjects had a titre of at least 1:80 at day 42.

#### Immune response against A/Indonesia/05/2005 (H5N1)

In a clinical study in which two doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Indonesia/05/2005 were administered on days 0 and 21 to 140 subjects aged 18-60 years, the anti-HA antibody responses were as follows:

anti-HA antibody	Immune response to A/Indonesia/05/2005		
	Day 21 N=140	Day 42 N=140	Day 180 N=138
Seroprotection rate <sup>1</sup>	45.7%	96.4%	49.3%
Seroconversion rate <sup>2</sup>	45.7%	96.4%	48.6%
Seroconversion factor <sup>3</sup>	4.7	95.3	5.2

<sup>1</sup>seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥1:40;

<sup>2</sup>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;

<sup>3</sup>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 79.2% of subjects twenty-one days after the first dose, 95.8% twenty-one days after the second dose and 87.5% six months after the second dose.

In a second study, 49 subjects aged 18-60 years received two doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Indonesia/05/2005 on days 0 and 21. At day 42, the anti-HA antibody seroconversion rate was 98%, all subjects were seroprotected and the seroconversion factor was 88.6. In addition, all subjects had neutralising antibody titres of at least 1:80.

#### Cross-reactive immune responses elicited by AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 (H5N1):

Anti-HA responses against A/Indonesia/5/2005 following administration of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 were as follows:

anti-HA antibody	A/Indonesia/5/2005	
	0, 21 days schedule	0, 6 months schedule

	21 days after 2 <sup>nd</sup> dose N = 924	7 days after 2 <sup>nd</sup> dose N = 47	21 days after 2 <sup>nd</sup> dose N = 48
Seroprotection rate* <sup>1</sup>	50.2%	74.5%	83.3%
Seroconversion rate <sup>2</sup>	50.2%	74.5%	83.3%
Seroconversion factor <sup>3</sup>	4.9	12.9	18.5

\* anti-HA  $\geq$ 1:40

<sup>1</sup> seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre  $\geq$ 1:40;

<sup>2</sup> seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of  $\geq$ 1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre;

<sup>3</sup> seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

A 4-fold increase in serum neutralising antibody against A/Indonesia/5/2005 was achieved in >90% of subjects after two doses regardless of the schedule. After two doses administered 6 months apart all subjects had a titre of at least 1:80.

In a different study in 50 subjects aged 18-60 years the anti-HA antibody seroprotection rates 21 days after the second dose of AS03-adjuvanted vaccine containing 3.75  $\mu$ g HA derived from A/Vietnam/1194/2004 were 20% against A/Indonesia/5/2005, 35% against A/Anhui/01/2005 and 60% against A/Turkey/Turkey/1/2005.

In 152 subjects aged > 60 years the anti-HA antibody seroprotection and seroconversion rates against A/Indonesia/5/2005 at day 42 after two doses of AS03-adjuvanted vaccine containing 3.75  $\mu$ g HA derived from A/Vietnam/1194/2004 were 23% and the seroconversion factor was 2.7. Neutralising antibody titres of at least 1:40 or at least 1:80 were achieved in 87% and 67%, respectively, of the 87 subjects tested.

Cross-reactive immune response elicited by AS03-adjuvanted vaccine containing 3.75  $\mu$ g HA derived from A/Indonesia/05/2005 (H5N1)

After two doses of AS03-adjuvanted vaccine containing 3.75  $\mu$ g HA derived from A/Indonesia/05/2005 administered on days 0 and 21 to 140 subjects aged 18-60 years, the anti-HA antibody responses to A/Vietnam/1194/2004 were as follows:

anti-HA antibody	Immune response to A/Vietnam/1194/2004	
	Day 21 N=140	Day 42 N=140
Seroprotection rate <sup>1</sup>	15%	59.3%
Seroconversion rate <sup>2</sup>	12.1%	56.4%
Seroconversion factor <sup>3</sup>	1.7	6.1

<sup>1</sup> seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre  $\geq$ 1:40;

<sup>2</sup> seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of  $\geq$ 1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre;

<sup>3</sup> seroconversion factor: ratio of the post-vaccination geometric mean titre (GMT) and the pre-vaccination GMT.

At day 180, the seroprotection rate was 13%.

A 4-fold increase in serum neutralising antibody titres against A/Vietnam was obtained in 49% of subjects twenty-one days after the first dose, 67.3% twenty-one days after the second dose and 44.9% six months after the second dose.



One dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Indonesia/05/2005 administered after one or two doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004.

In a clinical study, subjects aged 18-60 years received a dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from either A/Vietnam/1194/2004 or Indonesia/5/2005 six months after they had received one or two priming doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 on day 0 or on days 0 and 21 respectively. The anti-HA responses were as follows:

anti-HA antibody	Against A/Vietnam 21 days after boosting with A/Vietnam N=46		Against A/Indonesia 21 days after boosting with A/Indonesia N=49	
	After one priming dose	After two priming doses	After one priming dose	After two priming doses
Seroprotection rate <sup>1</sup>	89.6%	91.3%	98.1%	93.9%
Booster seroconversion rate <sup>2</sup>	87.5%	82.6%	98.1%	91.8%
Booster factor <sup>3</sup>	29.2	11.5	55.3	45.6

<sup>1</sup> seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre  $\geq 1:40$ ;

<sup>2</sup> booster seroconversion rate: proportion of subjects who were either seronegative at pre-booster and have a protective post-vaccination titre of  $\geq 1:40$ , or who were seropositive at pre-booster and have a 4-fold increase in titre;

<sup>3</sup> booster factor: ratio of the post-booster geometric mean titre (GMT) and the pre-booster GMT.

Regardless of whether one or two doses of priming vaccine had been given 6 months earlier, the seroprotection rates against A/Indonesia were  $>80\%$  after a dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 and the seroprotection rates against A/Vietnam were  $>90\%$  after a dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Indonesia/05/2005. All subjects achieved a neutralising antibody titre of at least 1:80 against each of the two strains regardless of the HA type in the vaccine and the previous number of doses.

In another clinical study, 39 subjects aged 18-60 years received a dose of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Indonesia/5/2005 fourteen months after they had received two doses of AS03-adjuvanted vaccine containing 3.75 µg HA derived from A/Vietnam/1194/2004 administered on day 0 and day 21. The seroprotection rate against A/Indonesia 21 days after booster vaccination was 92% and 69.2% at day 180.

#### 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-fetal 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 ( $\text{Na}_2\text{HPO}_4$ )

Potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )

Potassium chloride (KCl)

Magnesium chloride ( $\text{MgCl}_2$ )

Water for injections

*Emulsion vial:*

Sodium chloride (NaCl)

Disodium hydrogen phosphate ( $\text{Na}_2\text{HPO}_4$ )

Potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )

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**

Pandemrix 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 Pandemrix (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)**

EU/1/08/452/001

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 20/05/2008

## **10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) <http://www.emea.europa.eu/>.

## **ANNEX II**

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE  
SUBSTANCE AND MANUFACTURING AUTHORISATION  
HOLDER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OF THE MARKETING AUTHORISATION**
- C. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE  
MARKETING AUTHORISATION HOLDER**

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

Name and address of the manufacturer(s) of the biological active substance

GlaxoSmithKline Biologicals  
Branch of SmithKline Beecham Pharma GmbH & Co. KG  
Zirkustraße 40, D-01069 Dresden  
Germany

Name and address of the manufacturer(s) 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.

Pandemrix can only be marketed when there is an official WHO/EU declaration of an influenza pandemic, on the condition that the Marketing Authorisation Holder for Pandemrix takes due account of the officially declared pandemic strain.

**• 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 RMPv5 (dated March 2009) 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 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, during 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 pandemic vaccine is used, the MAH shall submit more frequent simplified periodic safety update reports with a format and a periodicity defined in the "CHMP Recommendations for the Core Risk Management Plan for Influenza Vaccines prepared from viruses with the potential to cause a pandemic and intended for use outside of the core dossier context" (EMEA/49993/2008), and any subsequent update.

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.

**C. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE MARKETING AUTHORISATION HOLDER**

The Marketing Authorisation Holder shall complete the following programme of studies within the specified time frame, the results of which shall form the basis of the annual reassessment of the benefit/risk profile in case the Pandemic will be declared.

Clinical	During the pandemic, the applicant will collect clinical safety and effectiveness data of the pandemic vaccine and submit this information to the CHMP for evaluation.	Depending on and after implementation of vaccine when first pandemic will take place.
Pharmacovigilance	During the pandemic, the applicant will conduct a prospective cohort study as identified in the Pharmacovigilance plan.	Depending on and after implementation of vaccine when first pandemic will take place.

**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**

Pandemrix suspension and emulsion for emulsion for injection.  
Pandemic 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 (10.69 milligrams), DL- $\alpha$ -tocopherol (11.86 milligrams) and polysorbate 80 (4.86 milligrams)

\* haemagglutinin

**3. LIST OF EXCIPIENTS**

Polysorbate 80  
Octoxynol 10  
Thiomersal  
Sodium chloride (NaCl)  
Disodium hydrogen phosphate ( $\text{Na}_2\text{HPO}_4$ )  
Potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )  
Potassium chloride (KCl)  
Magnesium chloride ( $\text{MgCl}_2$ )  
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/1/08/452/001

**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**

Pandemrix suspension for emulsion for injection  
Pandemic 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 ( $\text{Na}_2\text{HPO}_4$ )  
Potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )  
Potassium chloride (KCl)  
Magnesium chloride ( $\text{MgCl}_2$ )  
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)****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 Pandemrix

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

AS03 adjuvant composed of squalene (10.69 milligrams), DL- $\alpha$ -tocopherol (11.86 milligrams) and polysorbate 80 (4.86 milligrams)

**3. LIST OF EXCIPIENTS**

Sodium chloride (NaCl)  
Disodium hydrogen phosphate ( $\text{Na}_2\text{HPO}_4$ )  
Potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )  
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)****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  
Pandemrix 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 Pandemrix

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

### **Pandemrix suspension and emulsion for emulsion for injection** Pandemic 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 Pandemrix is and what it is used for
2. Before you receive Pandemrix
3. How Pandemrix is given
4. Possible side effects
5. How to store Pandemrix
6. Further information

#### **1.**

What Pandemrix is and what it is used for

Pandemrix is a vaccine for use in adults from 18 years old to prevent pandemic influenza (flu).

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, Pandemrix may not fully protect all persons who are vaccinated.

#### **2.**

Before you receive Pandemrix

#### **Pandemrix should not be given:**

- if you have previously had a sudden life-threatening allergic reaction to any ingredient of Pandemrix (these are listed at the end of the 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. However, in a pandemic situation, it may be appropriate for you to have the vaccine provided that appropriate medical treatment is immediately available in case of an allergic reaction.

Do not have Pandemrix if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before having this vaccine.

#### **Take special care with Pandemrix:**

- 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 a severe infection with a high temperature (over 38°C). If this applies to you then your vaccination will usually 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 Pandemrix.
- 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 Pandemrix the results of these tests may not be correct. Tell the doctor requesting these tests that you have recently received Pandemrix.

### **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.

Pandemrix 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, Pandemrix 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 Pandemrix in pregnant women. Your doctor needs to assess the benefits and potential risks of giving you the vaccine if you are pregnant. Please tell your doctor if you are/may be pregnant or intend to become pregnant.

Pandemrix may be given while you are breast-feeding.

### **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 Pandemrix**

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 Pandemrix is given

### **If you have not previously received doses of Prepandrix or Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals 3.75 µg**

- From 18 years onwards: you will receive two doses of Pandemrix. The second dose should be given after an interval of at least three weeks after the first dose.
- From 80 years onwards: you may receive two double injections of Pandemrix. The first two injections should be given at the elected date and the two other injections should preferably be given 3 weeks after.

**If you have previously received one or two doses of Prepandrix or Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) GlaxoSmithKline Biologicals 3.75 µg**

- From 18 years onwards: you will receive one dose of Pandemrix.

The doctor or nurse will give Pandemrix as an injection into your upper arm muscle. The vaccine should never be given into a vein or into the skin. The double injections will be given in opposite arms.

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

#### **4.**

##### Possible side effects

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

The side effects listed below have occurred in the days or weeks after vaccination with vaccines given routinely every year to prevent flu. These side effects may occur with Pandemrix.

##### **Very rare (these may occur with up to 1 in 10,000 doses of the vaccine):**

- Temporary inflammation of the brain and nerves causing pain, weakness and paralysis that may spread across the body.
- Narrowing or blockage of blood vessels with kidney problems

##### **Rare (these may occur with up to 1 in 1,000 doses of the vaccine):**

- Allergic reactions leading to a dangerous decrease of blood pressure, which, if untreated, may lead to collapse, coma and death
- Fits
- Severe stabbing or throbbing pain along one or more nerves
- Low blood platelet count which can result in bleeding or bruising

##### **Uncommon (these may occur with up to 1 in 100 doses of the vaccine):**

- Generalised skin reactions including urticaria (hives)

If any of these side effects occur, please tell your doctor or pharmacist immediately.

The side effects listed below have occurred with Pandemrix in clinical studies:

##### **Very common (these may occur with more than 1 in 10 doses of the vaccine):**

- Headache
- Tiredness
- 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
- Sleepiness
- Dizziness
- Diarrhoea, vomiting, stomach pain, feeling sick

- Itching, rash
- Generally feeling unwell
- Sleeplessness

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

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 Pandemrix

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 Pandemrix 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 (10.69 milligrams), DL- $\alpha$ -tocopherol (11.86 milligrams) and polysorbate 80 (4.86 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<sub>2</sub>HPO<sub>4</sub>), potassium dihydrogen phosphate (KH<sub>2</sub>PO<sub>4</sub>), potassium chloride (KCl), magnesium chloride (MgCl<sub>2</sub>), water for injections

#### **What Pandemrix looks like and contents of the pack**

One pack of Pandemrix consists of:

- one pack containing 50 vials of 2.5 ml suspension (antigen) 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**

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

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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

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

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

Pandemrix 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 Pandemrix (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.