ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Pandemic influenza vaccine H5N1 AstraZeneca nasal spray, suspension
Pandemic influenza vaccine (H5N1) (live attenuated, nasal)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.2 ml) contains:

Reassortant influenza virus* (live attenuated) of the following strain**:

A/Vietnam/1203/2004 (H5N1) strain
(A/Vietnam/1203/2004, MEDI 0141000136) $10^{7.0\pm0.5}$ FFU***

* propagated in fertilised hens' eggs from healthy chicken flocks.
** produced in VERO cells by reverse genetic technology. This product contains a genetically modified organism (GMO).
*** fluorescent focus units

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

The vaccine may contain residues of the following substances: egg proteins (e.g. ovalbumin) and gentamicin. The maximum amount of ovalbumin is less than 0.024 micrograms per 0.2 ml dose (0.12 micrograms per ml).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nasal spray, suspension

The suspension is colourless to pale yellow, clear to opalescent with a pH of approximately 7.2. Small white particles may be present.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of influenza in an officially declared pandemic situation in children and adolescents from 12 months to less than 18 years of age.

Pandemic influenza vaccine H5N1 AstraZeneca should be used in accordance with official guidance.

4.2 Posology and method of administration

Posology
Children and adolescents from 12 months to less than 18 years of age
0.2 ml (administered as 0.1 ml per nostril).
Two doses are recommended for all children and adolescents. The second dose should be administered after an interval of at least 4 weeks.

Children less than 12 months
Pandemic influenza vaccine H5N1 AstraZeneca should not be used in infants below 12 months of age because of safety concerns regarding increased rates of hospitalisation and wheezing in this population (see section 4.8).

Method of administration
Immunisation must be carried out by nasal administration.

Do not inject Pandemic influenza vaccine H5N1 AstraZeneca.

Pandemic influenza vaccine H5N1 AstraZeneca is administered as a divided dose in both nostrils. After administering half of the dose in one nostril, administer the other half of the dose in the other nostril immediately or shortly thereafter. The patient can breathe normally while the vaccine is being administered – there is no need to actively inhale or sniff.

See section 6.6 for administration instructions.

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to the active substance or to any of the excipients listed in section 6.1 (e.g. gelatin), or to gentamicin (a possible trace residue), to eggs or to egg proteins (e.g. ovalbumin). 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.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Caution is needed when administering this vaccine to individuals with a known hypersensitivity (other than anaphylactic reaction) to the active substance, or to any of the excipients listed in section 6.1, or to trace residues (gentamicin, eggs or egg proteins, ovalbumin). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event or hypersensitivity event following administration of the vaccine.

There are no data with Pandemic influenza vaccine H5N1 AstraZeneca in children and adolescents younger than 18 years of age receiving salicylate therapy. Due to the association of Reye's syndrome with salicylates and wild-type influenza infection, healthcare providers should assess the potential risks of administering the vaccine with the potential benefits in a pandemic situation (see section 4.5).

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

No data are available for individuals with significant clinical immunodeficiency. In a pandemic situation, healthcare providers need to assess the potential benefits, alternatives, and risks of administering the vaccine to children and adolescents with significant clinical immunodeficiency due to conditions or immunosuppressive therapy such as: acute and chronic leukaemias; lymphoma; symptomatic HIV infection; cellular immune deficiencies; and high-dose corticosteroids.

The safety of seasonal live attenuated influenza vaccine (LAIV) in children with severe asthma and active wheezing has not been adequately studied. Healthcare providers need to assess the benefits and potential risks of administering Pandemic influenza vaccine H5N1 AstraZeneca to these individuals.

In a study with the seasonal trivalent live attenuated influenza vaccine (T/LAIV), an increased incidence of medically significant wheezing was seen in children 12-23 months of age (see section 4.8).

Vaccine recipients should be informed that Pandemic influenza vaccine H5N1 AstraZeneca is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1-2 weeks following vaccination. Shedding of the H5N1 vaccine virus in adults was extremely limited. Peak incidence of vaccine virus recovery occurred 1-2 days post-vaccination in clinical studies with Pandemic influenza vaccine H5N1 AstraZeneca. In circumstances where contact with severely immunocompromised individuals is unavoidable, the potential risk of transmission of the influenza vaccine virus should be weighed against the risk of acquiring and transmitting wild-type influenza virus.

Vaccine recipients under treatment with influenza antiviral agents should not receive Pandemic influenza vaccine H5N1 AstraZeneca until 48 hours after the cessation of influenza antiviral therapy.

No data exist regarding the safety of intranasal administration of Pandemic influenza vaccine H5N1 AstraZeneca in children with unrepaired craniofacial malformations.

4.5 Interaction with other medicinal products and other forms of interaction

Children and adolescents under 18 years of age receiving salicylate therapy should avoid vaccination with Pandemic influenza vaccine H5N1 AstraZeneca (see section 4.4). Use of salicylates in children and adolescents for 4 weeks after vaccination should be avoided unless medically indicated as Reye's syndrome has been reported following the use of salicylates during wild-type influenza infection.

The co-administration of Pandemic influenza vaccine H5N1 AstraZeneca with inactivated vaccines or with the seasonal vaccine Fluenz Tetra has not been studied.

Data regarding co-administration of the seasonal trivalent influenza vaccine live, intranasal (T/LAIV) with live attenuated vaccines (measles, mumps, and rubella vaccine (MMR), varicella vaccine, and orally-administered poliovirus) are available and suggest that concomitant admininstration of Pandemic influenza vaccine H5N1 AstraZeneca with these live vaccines may be acceptable.

Based upon the potential for influenza antiviral agents to reduce the effectiveness of Pandemic influenza vaccine H5N1 AstraZeneca, it is recommended not to administer the vaccine until 48 hours after the cessation of influenza antiviral therapy. Administration of influenza antiviral agents within two weeks of vaccination may affect the response of the vaccine.

If influenza antiviral agents and Pandemic influenza vaccine H5N1 AstraZeneca are administered concomitantly, timing and the need for revaccination should be considered based on clinical judgement.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data available on the use of Pandemic influenza vaccine H5N1 AstraZeneca in pregnant women.

There are a moderate amount of data from the use of T/LAIV and the seasonal Fluenz Tetra vaccine in pregnant women. There was no evidence of significant maternal adverse outcomes in 138 pregnant women who had a record of receiving the seasonal T/LAIV vaccine in a US-based health insurance claims database.

In more than 300 case reports in the AstraZeneca safety database of vaccine administration in pregnant women, no unusual patterns of pregnancy complications or foetal outcomes were observed. Similarly from the VAERS, in 113 reports of pregnant women who had received AstraZeneca's (H1N1) 2009 Monovalent Vaccine Live, Intranasal, no unusual patterns of pregnancy complications or foetal outcomes were observed.

Animal developmental toxicity studies conducted with T/LAIV and Fluenz Tetra do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Post-marketing data from occasional inadvertent gestational use of the seasonal vaccines offer some reassurance.

Healthcare providers need to assess the benefit and potential risks of administering Pandemic influenza vaccine H5N1 AstraZeneca to pregnant women.

Breast-feeding
It is not known whether Pandemic influenza vaccine H5N1 AstraZeneca is excreted in human milk. Therefore, as some viruses are excreted in human milk, the vaccine should not be used during breast-feeding.

Fertility
No data exist regarding the possible effects of Pandemic influenza vaccine H5N1 AstraZeneca on male and female fertility.

4.7 Effects on ability to drive and use machines

Pandemic influenza vaccine H5N1 AstraZeneca has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The assessment of the safety profile for Pandemic influenza vaccine H5N1 AstraZeneca is based on a limited number of adult subjects.

In clinical studies, the safety profile of Pandemic influenza vaccine H5N1 AstraZeneca was comparable to the safety profile of the seasonal vaccines T/LAIV and Fluenz Tetra (see section 5.1 for more information).

Clinical studies have evaluated the incidence of adverse reactions in 59 adults from 18 to 49 years of age receiving at least one dose of Pandemic influenza vaccine H5N1 AstraZeneca. Additional data are provided from 289 adults enrolled in studies of vaccine candidates for an additional 7 influenza subtypes and from 240 adults and 259 children enrolled in studies of the monovalent 2009 H1N1 pandemic vaccine.

The most common adverse reactions observed in clinical studies conducted with the Pandemic influenza vaccine H5N1 AstraZeneca in healthy adults was headache (25.4%) and upper respiratory infection (10.2%).

Paediatric population

List of adverse reactions
From clinical studies and post-marketing surveillance with T/LAIV and Fluenz Tetra in over 110,000 children and adolescents 2 to 17 years of age, the following adverse reaction frequencies are reported:
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)

Immune system disorders
Uncommon: Hypersensitivity reactions (including facial oedema, urticaria and very rare anaphylactic reactions)

Metabolism and nutrition disorders
Very common: Decreased appetite

Nervous system disorders
Common: Headache

Respiratory, thoracic and mediastinal disorders
Very common: Nasal congestion/rhinorrhoea
Uncommon: Epistaxis

Skin and subcutaneous tissue disorders
Uncommon: Rash

Musculoskeletal and connective tissue disorders
Common: Myalgia

General disorders and administration site conditions
Very common: Malaise
Common: Pyrexia

Description of selected adverse reactions

Children less than 12 months of age
Pandemic influenza vaccine H5N1 AstraZeneca is not indicated for use in infants younger than 12 months of age (see section 4.2). The safety and efficacy of the vaccine in this population has not been established. No data are available.

In an active-controlled clinical study (MI-CP111) conducted with T/LAIV in comparison to the injectable influenza trivalent vaccine, an increased rate of hospitalisations (for any cause) through 180 days after final vaccination dose was observed in infants 6-11 months of age (6.1% T/LAIV versus 2.6% injectable influenza vaccine). Most hospitalisations were due to gastrointestinal and respiratory tract infections and occurred more than 6 weeks post vaccination. The rate of hospitalisations was not increased in T/LAIV recipients 12 months and older and the rates for infants and toddlers 12-23 months of age were 3.2% T/LAIV versus 3.5% injectable influenza vaccine.

Wheezing in children below 24 months of age
In the same study, an increased rate of wheezing through 42 days was observed in infants and toddlers 6-23 months of age (5.9% T/LAIV versus 3.8% injectable influenza vaccine). Corresponding rates for infants and toddlers 12-23 months of age were 5.4% and 3.6% for T/LAIV and injectable influenza vaccine, respectively. A total of 20 subjects (12 T/LAIV, 0.3%; 8 injectable influenza vaccine, 0.2%) were hospitalised in association with medically significant wheezing. No deaths resulted from these events, and none of the hospitalised children required mechanical ventilation or admission to an intensive care unit. The rate of wheezing was not increased in T/LAIV recipients 24 months of age and older.

Chronic conditions
Although safety in children and adolescents with mild to moderate asthma has been established for T/LAIV, data in children with other pulmonary diseases or with chronic cardiovascular, metabolic or renal diseases are limited.

In a study (D153-P515) of children 6 to 17 years of age with asthma (seasonal T/LAIV: n=1,114, seasonal injectable influenza vaccine: n=1,115), there were no significant differences between treatment groups in the incidence of asthma exacerbations, mean peak expiratory flow rate, asthma symptom scores, or night-time awakening scores. The incidence of wheezing within 15 days after vaccination was lower in T/LAIV recipients relative to seasonal inactivated vaccine recipients (19.5% vs. 23.8%, P=0.02).

In a study (AV010) of children and adolescents 9 to 17 years of age with moderate to severe asthma (seasonal T/LAIV: n=24, placebo: n=24), the primary safety criterion, change in percent predicted forced expiratory volume in 1 second (FEV_1) measured before and after vaccination, did not differ between treatment arms.

Other special populations:

Immunocompromised
Overall, the safety profile of T/LAIV in a limited number of subjects with mildly to moderately non-HIV related compromised immune function, asymptomatic or mildly symptomatic HIV infection, or cancer (solid tumors and haematological malignancies) was comparable to that in healthy individuals and does not indicate any untoward effect. No data are available for individuals with severe immunosuppression (see section 4.4). In a pandemic situation, the use of Pandemic influenza vaccine H5N1 AstraZeneca in mildly to moderately immunosuppressed individuals may be considered after weighing the anticipated benefits against the potential risks for the individual.

Post-marketing experience with seasonal T/LAIV
Very rare reports of Guillain-Barré syndrome and exacerbation of symptoms of Leigh syndrome (mitochondrial encephalomyopathy) have also been observed.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Administration of a higher than recommended dose of Pandemic influenza vaccine H5N1 AstraZeneca has not been reported in the small number of subjects who received the vaccine during pre-licensure clinical studies. Based on experience with the live attenuated seasonal influenza vaccine, administration of a higher than recommended dose is expected to result in an adverse reaction profile that is comparable to that observed with the recommended dose of Pandemic influenza vaccine H5N1 AstraZeneca.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccines, influenza live attenuated; ATC Code: J07BB03

The influenza virus strain in Pandemic influenza vaccine H5N1 AstraZeneca is (a) *cold-adapted (ca)*; (b) *temperature-sensitive (ts)*; and (c) *attenuated (att)*. The virus must infect and replicate in cells lining the nasopharynx of the vaccine recipient in order to induce protective immunity.

Clinical studies

This section describes the clinical experience observed in three pivotal studies conducted with the Pandemic influenza vaccine H5N1 AstraZeneca in adults. In addition, studies conducted with AstraZeneca's 2009 H1N1 pandemic LAIV and seasonal T/LAIV vaccine are also considered supportive because all these vaccines are manufactured using the same process, administered through the same route, and studied primarily in naïve individuals.

Paediatric studies

H1N1 pandemic LAIV vaccine in children aged 2 to 17 years

In clinical study MI-CP217, the safety and descriptive immunogenicity of a live attenuated monovalent influenza virus vaccine (derived from A/California/7/2009) developed for the 2009 H1N1 pandemic were evaluated in a total of 326 randomised subjects (259 subjects monovalent vaccine; 65 subjects placebo) and 324 subjects received one dose of investigational product. Of these subjects, 319 received a second dose (256 subjects monovalent vaccine; 63 subjects placebo).

For children regardless of baseline serostatus, seroresponse rates after receipt of monovalent vaccine were 7.8% and 11.1% for Days 15 and 29, respectively, and 32.0% on Day 57. For placebo recipients regardless of baseline serostatus, seroresponse rate was 6.3% on Days 15 and 29 and 14.5% on Day 57. Seroresponse rates were slightly higher among subjects who were seronegative at baseline. In a surveillance study conducted by the US CDC (Griffin, et al, 2011) the effectiveness of the H1N1 pandemic LAIV vaccine in children 2 through 9 years of age was estimated at 81.9% (95% CI:13.6, 96.2).

T/LAIV efficacy

T/LAIV's efficacy data in the paediatric population consist of 9 controlled studies comprising over 20,000 infants and toddlers, children and adolescents, conducted during 7 influenza seasons. Four placebo-controlled studies included second season revaccination. T/LAIV has demonstrated superiority in 3 active-controlled studies with injectable influenza vaccine. See Table 1 and 2 for a summary of efficacy results in the paediatric population.

Table 1 T/LAIV efficacy in placebo controlled paediatric studies

Study number	**Region**	**Age range[a]**	**Number of study participants[b]**	**Influenza season**	**Efficacy (95% CI)[c] matched strains**	**Efficacy (95% CI)[c] all strains regardless of match**
D153-P502	Europe	6 to 35 M	1,616	2000-2001	85.4% (74.3, 92.2)	85.9% (76.3, 92.0)
			1,090	2001-2002	88.7% (82.0, 93.2)	85.8% (78.6, 90.9)
D153-P504	Africa, Latin America	6 to 35 M	1,886	2001	73.5% (63.6, 81.0)[d]	72.0% (61.9, 79.8)[d]
			680	2002	73.6% (33.3, 91.2)	46.6% (14.9, 67.2)
D153-P513	Asia/ Oceania	6 to 35 M	1,041	2002	62.2% (43.6, 75.2)	48.6% (28.8, 63.3)
D153-P522	Europe, Asia/ Oceania, Latin America	11 to 24 M	1,150	2002-2003	78.4% (50.9, 91.3)	63.8% (36.2, 79.8)

D153-P501	Asia/ Oceania	12 to 35 M	2,764	2000-2001	72.9% (62.8, 80.5)	70.1% (60.9, 77.3)
			1,265	2001-2002	84.3% (70.1, 92.4)[e]	64.2% (44.2, 77.3)[e]
AV006	USA	15 to 71 M	1,259	1996-1997	93.4% (87.5, 96.5)	93.4% (87.5, 96.5)
			1.358	1997-1998	100% (63.1, 100)	87.1% (77.7, 92.6)[f]

[a]M = months
[b]Number of study participants for year 1 or year 2 primary efficacy analysis.
[c]Reduction in culture-confirmed influenza illness relative to placebo.
[d]Data presented for clinical trial D153-P504 are for study participants who received two doses of study vaccine or placebo. In previously unvaccinated study participants who received one dose in year 1, efficacy was 57.7% (95% CI: 44.7, 67.9) against matched strains and 56.3% (95% CI: 43.1, 66.7) against all strains regardless of match, respectively, thus supporting the need for two doses of vaccine in previously unvaccinated children.
[e]In study participants who received 2 doses in year 1 and placebo in year 2, efficacy in year 2 was 56.2% (95% CI: 30.5, 72.7) against matched strains and 44.8% (95% CI: 18.2, 62.9) against all strains regardless of match, respectively, in D153-P501, thus supporting the need for second-season revaccination.
[f]The primary circulating strain was antigenically dissimilar from the H3N2 strain represented in the vaccine; efficacy against the mismatched A/H3N2 strain was 85.9% (95% CI: 75.3, 91.9).

Table 2 T/LAIV relative efficacy in active-controlled paediatric studies with seasonal injectable influenza vaccine

Study number	**Region**	**Age range[a]**	**Number of study participants**	**Influenza season**	**Improved efficacy (95% CI)[b] matched strains**	**Improved efficacy (95% CI)[b] all strains regardless of match**
MI-CP111	USA, Europe, Asia/Oceania	6 to 59 M	7,852	2004-2005	44.5% (22.4, 60.6) fewer cases than injectable	54.9% (45.4, 62.9)[c] fewer cases than injectable
D153-P514	Europe	6 to 71 M	2,085	2002-2003	52.7% (21.6, 72.2) fewer cases than injectable	52.4% (24.6, 70.5)[d] fewer cases than injectable
D153-P515	Europe	6 to 17 Y	2,211	2002-2003	34.7% (3.9, 56.0) fewer cases than injectable	31.9% (1.1, 53.5) fewer cases than injectable

[a]M = months. Y = years. Age range as described in the protocol for the study.
[b]Reduction in culture-confirmed influenza illness relative to injectable influenza vaccine.
[c]T/LAIV demonstrated 55.7% (39.9, 67.6) fewer cases than injectable influenza vaccine in 3,686 infants and toddlers 6-23 months of age and 54.4% (41.8, 64.5) fewer cases in 4,166 children 24-59 months of age.
[d]T/LAIV demonstrated 64.4% (1.4, 88.8) fewer cases than injectable influenza vaccine in 476 infants and toddlers 6-23 months of age and 48.2% (12.7, 70.0) fewer cases in 1,609 children 24-71 months of age.

P/LAIV H5N1 vaccine

The European Medicines Agency has deferred the obligation to submit the results of studies with Pandemic influenza vaccine H5N1 AstraZeneca in one or more subsets of the paediatric population in prevention of influenza infection. See section 4.2 for information on paediatric use.

This medicinal product has been authorised under a so-called ‘conditional approval’ scheme. This means that further evidence on this medicinal product is awaited. The European Medicines Agency will review any new information on the product every year and this SmPC will be updated as necessary.

Adult studies

Adults aged 18 to 49 years

In clinical study CIR 217, the safety, infectivity and immunogenicity of a live attenuated vaccine derived from A/Vietnam/1203/2004 (H5N1) influenza isolate were evaluated in 21 subjects who received one $10^{6.7}$ median tissue culture infectious dose ($TCID_{50}$), with 18 of those subjects receiving a second dose 4-8 weeks later. Twenty-one additional subjects received one dose of the vaccine virus at $10^{7.5}$ $TCID_{50}$, with 19 of those subjects receiving a second dose 4-8 weeks later. After 1 or 2 doses of $10^{6.7}$ $TCID_{50}$ vaccine, haemagglutination inhibition (HAI) and IgA seroresponses were each detected in 10% subjects, and nasal wash IgA responses were detected in 24% subjects. After 1 or 2 doses of $10^{7.5}$ $TCID_{50}$ vaccine, HAI and IgA seroresponses were each detected in 10% and 52% of subjects and nasal IgA responses were detected in 19% of subjects.

In clinical study CIR 239, the safety, infectivity, and immunogenicity of a live attenuated vaccine derived from A/Hong Kong/213/2003 (H5N1) influenza isolate were evaluated in 17 subjects who received one dose of $10^{7.5}$ $TCID_{50}$ of the vaccine intranasally in isolation, with 16 of those subjects receiving a second dose 4-8 weeks later. HAI responses were not detected in any of the subjects after either the first or second dose of the vaccine. IgA seroresponse and nasal wash response were each detected in 18% of subjects.

Adults aged 22 to 54 years

Clinical study CIR 277 assessed whether prior recipients of pandemic live attenuated influenza H5N1 vaccines were primed or established long-lasting immunity that could be detected following the subsequent administration of an inactivated H5N1 vaccine. The study enrolled 69 subjects in 5 groups: Group 1 enrolled 11 subjects who had previously received 2 doses of the A/Vietnam/1203/2004 H5N1 pandemic live attenuated influenza vaccine (P/LAIV) in 2006-2007; Group 2 enrolled 10 subjects who had previously received 2 doses of the A/Hong Kong/213/2003 H5N1 P/LAIV in 2007; Group 3 enrolled 8 subjects who had previously received 2 doses of the A/British Columbia/CN-6/2004 H7N3 P/LAIV in 2010 (as a P/LAIV control group); Groups 4 and 5 each enrolled 20 subjects who had not been previously vaccinated with LAIV and were influenza H5 naïve. Subjects in Groups 1 to 4 received a single 45-µg dose of the A/Vietnam/1203/2004 pandemic inactivated influenza vaccine (P/IIV) while subjects in Group 5 received 2 doses, approximately 28 days apart.

P/LAIV H5N1-primed subjects developed vigorous antibody responses to wild-type H5N1 virus upon subsequent exposure to the inactivated H5N1 vaccine, although such antibody responses were not detectable after the primary 2 doses in the majority of the subjects. Subjects who were primed with either the A/Vietnam/1203/2004 P/LAIV or the A/Hong Kong/213/2003 P/LAIV had a significantly better response to a single dose of inactivated H5N1 vaccine than P/LAIV-naïve subjects. The antibody response in A/Vietnam/1203/2004 P/LAIV-primed subjects also exceeded that observed after 2 doses of inactivated vaccine in P/LAIV-naïve subjects (see Table 3).

Table 3 Serum microneutralization (MN) and haemagglutination inhibition (HAI) assay antibody responses on Days 28 and 56 following administration of an inactivated H5N1 vaccine

Study group	P/LAIV priming dose	Number of Vietnam 2004 inactivated vaccine doses	Number of subjects	28 Days after inactivated vaccine[a]				56 Days after inactivated vaccine[a]			
				Geometric mean titer		Subjects with 4-fold antibody rise (percentage)[b]		Geometric mean titer		Subjects with 4-fold antibody rise (percentage)[b]	
				MN	HAI	MN	HAI	MN	HAI	MN	HAI
1	H5N1 Vietnam 2004	1	11	48	87	73	73	25	66	55	82
2	H5N1 Hong Kong 2003	1	10	31	29	60	50	22	21	60	40
4	None	1	20	7	8	10	10	4	8	10	10
5	None	2	20[c]	11	15	30	40	19	21	56	50

Data for Group 3, subjects initially vaccinated with an H7N3 P/LAIV are not shown.
[a]Days are counted relative to the only P/IIV dose for Groups 1-4 and after the first of 2 P/IIV doses for Group 5.
[b]Serological response defined as a ≥4-fold rise in antibody titer (≥1:20).
[c]Serum samples were available from 7 subjects in Group 3 on Day 28 and from 18 subjects in Group 5 on Day 56.

Antibody response developed rapidly in P/LAIV H5N1-primed subjects. Seven of 11 (64%) subjects in Group 1 (ca A/Vietnam/1204/2004 [H5N1]) had ≥4-fold rises in HAI antibody titer by Day 7 following receipt of the inactivated vaccine, with a geometric mean titer (GMT) of 165 and a titer range of 20 to 1280 in responders. Of the P/LAIV-naïve subjects, only 10% had ≥4-fold rises by Day 7. Antibody responses in P/LAIV H5N1-primed subjects were also broader. H5N1 P/LAIV-primed subjects developed antibody responses that neutralised 2 or more clades of H5N1 viruses from the A/Goose/Guangdong/1996 H5N1 lineage, whereas few subjects even in the 2-dose inactivated H5N1 vaccine group developed cross-clade neutralising antibodies. The affinity of antibodies against the HA1 domain of the H5 HA in the H5N1 P/LAIV-primed groups was significantly higher than the 2-dose inactivated vaccine group, which correlated with cross-clade H5N1 neutralisation.

Similar responses were seen with P/LAIV H7N7- and H7N9-primed subjects who developed vigorous antibody responses to the corresponding wild-type viruses upon subsequent exposure to the inactivated vaccine from the same subtype. For the H7N7 P/LAIV, strong serum antibody responses were detected by both MN and HAI in 9 of 13 individuals, with peak titers achieved by Day 14. For the H7N9 P/LAIV, 8 of 14 individuals who received a single dose of vaccine and 13 of 16 individuals who received two doses of vaccine developed strong antibody responses; peak titers were again seen by Day 14.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data with the Pandemic influenza vaccine H5N1 AstraZeneca, and the seasonal vaccines T/LAIV and Fluenz Tetra reveal no special hazard for humans based on conventional non-clinical studies of repeated dose toxicity, reproduction and developmental toxicity, local tolerance, and neurovirulence.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Dipotassium phosphate
Potassium dihydrogen phosphate
Gelatin (porcine, Type A)
Arginine hydrochloride
Monosodium glutamate monohydrate
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

18 weeks.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Keep the nasal applicator in the outer carton in order to protect from light.

Before use, the vaccine may be taken out of the refrigerator once for a maximum period of 12 hours at a temperature not above 25°C. Stability data indicate that the vaccine components are stable for 12 hours when stored at temperatures from 8°C to 25°C. At the end of this period, Pandemic influenza vaccine H5N1 AstraZeneca should be used immediately or discarded.

6.5 Nature and contents of container

Pandemic influenza vaccine H5N1 AstraZeneca is supplied as a 0.2 ml suspension in a single-use nasal applicator (Type 1 glass), with nozzle (polypropylene with polyethylene transfer valve), nozzle tip-protector cap (synthetic rubber), plunger rod, plunger-stopper (butyl rubber), and a dose-divider clip.

Pack size of 10.

6.6 Special precautions for disposal and other handling

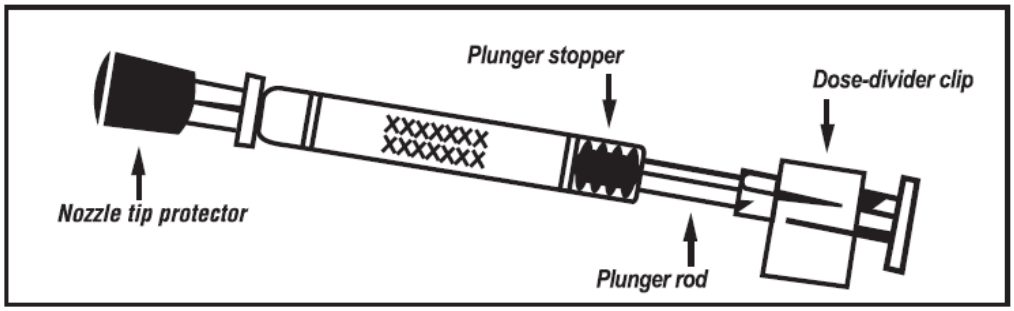
Administration

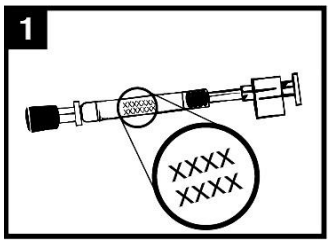
Pandemic influenza vaccine H5N1 AstraZeneca IS FOR NASAL USE ONLY.

- DO NOT USE WITH A NEEDLE. Do not inject.

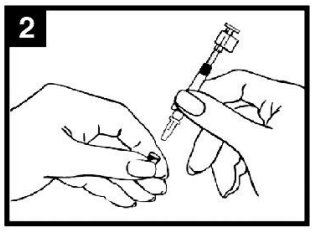
- Do not use Pandemic influenza vaccine H5N1 AstraZeneca if the expiry date has passed or if the sprayer appears damaged, for example, if the plunger is loose or displaced from the sprayer or if there are any signs of leakage.
- Check the appearance of the vaccine before administration. The suspension should be colourless to pale yellow, clear to opalescent. Small white particles may be present.
- Pandemic influenza vaccine H5N1 AstraZeneca is administered as a divided dose in both nostrils.
- After administering half of the dose in one nostril, administer the other half of the dose in the other nostril immediately or shortly thereafter.
- The patient can breathe normally while the vaccine is being administered – there is no need to actively inhale or sniff.
- Refer to the Pandemic influenza vaccine H5N1 AstraZeneca administration diagram (Figure 1) for step-by-step administration instructions.

Figure 1 Pandemic influenza vaccine H5N1 AstraZeneca Administration

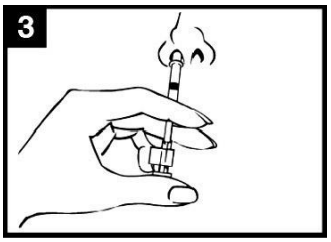




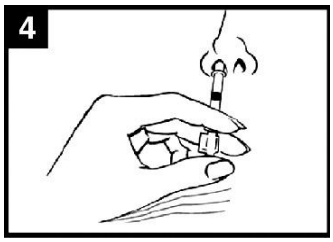
Check expiry date
Product must not be used after date on applicator label.



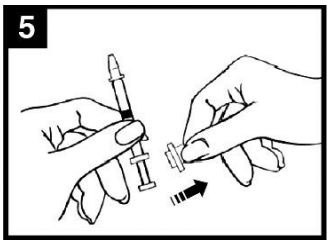
Prepare the applicator
Remove rubber tip protector. Do not remove dose-divider clip at the other end of the applicator.



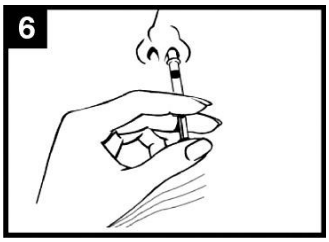
Position the applicator
With the patient in an upright position, place the tip just inside the nostril to ensure Pandemic influenza vaccine H5N1 AstraZeneca is delivered into the nose.



Depress the plunger
With a single motion, depress plunger **as rapidly as possible** until the dose-divider clip prevents you from going further.



Remove dose-divider clip
For administration in the other nostril, pinch and remove the dose-divider clip from plunger.



Spray in other nostril
Place the tip just **inside the other nostril** and with a single motion, depress plunger **as rapidly as possible** to deliver remaining vaccine.

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

7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1089/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 May 2016
Date of latest renewal: 19 April 2024

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

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

Name and address of the manufacturer of the biological active substance

MedImmune UK Limited
Plot 6, Renaissance Way
Boulevard Industry Park
Speke
Liverpool L24 9JW
United Kingdom

Name and address of the manufacturers responsible for batch release

AstraZeneca Nijmegen B.V.,
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

MedImmune UK Limited
Plot 6, Renaissance Way
Boulevard Industry Park
Speke
Liverpool L24 9JW
United Kingdom

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a State laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in Article 9 of Regulation (EC) No 507/2006 and, accordingly, the marketing authorisation holder (MAH) shall submit PSURs every 6 months.

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Not applicable

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14(7) of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
Non-interventional post-authorisation safety study (PASS) in order to further investigate the tolerability of Pandemic influenza vaccine H5N1 AstraZeneca and estimate the incidence of adverse reactions of special interest in children and adolescents. The MAH should conduct an observational prospective cohort safety study in a large sample of children and adolescents from 12 months to less than 18 years of age during the next declared pandemic. The MAH should submit the final results of this study.	After declaration in the EU of a pandemic and after implementation of the pandemic vaccine
In order to further corroborate the efficacy of Pandemic influenza vaccine H5N1 AstraZeneca, the MAH should conduct an observational effectiveness study in community dwelling children and adolescents from 12 months to less than 18 years of age against laboratory confirmed influenza during the next declared pandemic. The MAH should submit the final results of this study.	After declaration in the EU of a pandemic and after implementation of the pandemic vaccine
In order to further investigate the safety and reactogenicity of Pandemic influenza vaccine H5N1 AstraZeneca, the MAH should conduct an open-label single arm interventional study to evaluate the safety and immunogenicity of P/LAIV in children and adolescents from 12 months to less than 18 years of age during the next declared pandemic. The MAH should submit the final results of this study.	After declaration in the EU of a pandemic and after implementation of the pandemic vaccine
In order to define the shelf life of Pandemic influenza vaccine H5N1 AstraZeneca on a strain-specific basis, the MAH should generate strain-specific stability data for the actual pandemic strain. The MAH should submit the final results of this study.	At the time of approval of the next pandemic variation

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PACK SIZE OF 10 SINGLE-USE NASAL APPLICATORS

1. NAME OF THE MEDICINAL PRODUCT

Pandemic influenza vaccine H5N1 AstraZeneca nasal spray, suspension
Pandemic influenza vaccine (H5N1) (live attenuated, nasal)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Reassortant influenza virus (live attenuated) of the following strain:

A/Vietnam/1203/2004 (H5N1) strain
(A/Vietnam/1203/2004, MEDI 0141000136) $10^{7.0\pm0.5}$ FFU per 0.2 ml dose

3. LIST OF EXCIPIENTS

Excipients: sucrose, dipotassium phosphate, potassium dihydrogen phosphate, gelatin (porcine, Type A), arginine hydrochloride, monosodium glutamate monohydrate, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Nasal spray, suspension
10 single-use nasal applicators (0.2 ml each)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For nasal use only. Do not inject.
Read the package leaflet before use.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

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

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1089/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SINGLE-USE NASAL APPLICATOR

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

Pandemic influenza vaccine H5N1 AstraZeneca

2. METHOD OF ADMINISTRATION

For nasal use only.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.2 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Pandemic influenza vaccine H5N1 AstraZeneca, nasal spray suspension
Pandemic influenza vaccine (H5N1) (live attenuated, nasal)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before the vaccine is given because it contains important information for you or your child.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or pharmacist.
- This vaccine has been prescribed for you or your child only. Do not pass it on to others.
- If any of the side effects gets serious, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Pandemic influenza vaccine H5N1 AstraZeneca is and what it is used for

Pandemic influenza vaccine H5N1 AstraZeneca is a vaccine to prevent influenza (flu) in an officially declared pandemic. It is used in children and adolescents 12 months to less than 18 years of age.

Pandemic flu is a type of influenza that happens at intervals that vary from less than 10 years to many decades. It spreads rapidly around the world. The signs of pandemic flu are similar to those of ordinary flu but may be more serious.

How Pandemic influenza vaccine H5N1 AstraZeneca works

Pandemic influenza vaccine H5N1 AstraZeneca is similar to Fluenz Tetra (a nasal influenza vaccine containing four strains), except Pandemic influenza vaccine H5N1 AstraZeneca provides protection against a single influenza strain in an officially declared pandemic.

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

Pandemic influenza vaccine H5N1 AstraZeneca vaccine virus is grown in chicken eggs. The influenza strain used for the vaccine in an offically declared pandemic is recommended by the World Health Organisation.

2. What you need to know before you are given Pandemic influenza vaccine H5N1 AstraZeneca

You should not be given Pandemic influenza vaccine H5N1 AstraZeneca:

- **if you have previously had a serious allergic reaction (i.e. life-threatening)** to eggs, egg proteins, gentamicin, or gelatin or any of the other ingredients of this vaccine (listed in section 6 "Contents of the pack and other information"). For signs of allergic reactions, see section 4 "Possible side effects". However, in a pandemic situation, your doctor may recommend to give you the vaccine provided that appropriate medical treatment is immediately available in case of an allergic reaction.

If any of these apply, **tell your doctor, nurse or pharmacist**.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before vaccination:
- if the **child is less than 12 months of age**. Children less than 12 months of age should not receive this vaccine because of the risk of side effects.
- if you have had **any allergic reaction other than a sudden life-threatening allergic reaction** to eggs, egg proteins, gentamicin, or gelatin or any of the other ingredients of this vaccine (listed in section 6 "Contents of the pack and other information").
- if you are **already taking *acetylsalicylic acid*** (a substance present in many medicines used to relieve pain and lower fever). This is because of the risk of a very rare but serious disease *(Reye's syndrome)*.
- if you have a **blood disorder** or a **cancer** that **affects the immune system**.
- if you have been **told by your doctor** that you have **a weakened immune system** as a result of a disease, medicine, or other treatment.
- if you have **severe asthma** or are currently wheezing.
- if you are in **close contact with someone with a severely weakened immune system** (for example, a bone marrow transplant patient needing isolation).

If any of these apply, **tell your doctor, nurse or pharmacist before vaccination**. He or she will decide if Pandemic influenza vaccine H5N1 AstraZeneca is suitable for you.

Other medicines, other vaccines and Pandemic influenza vaccine H5N1 AstraZeneca
Tell your doctor, nurse or pharmacist if the person being vaccinated is taking, has recently taken or might take any other medicines, including medicines that do not require a prescription.
- **Do not give acetylsalicylic acid** (a substance present in many medicines used to relieve pain and lower fever) **to children** for 4 weeks after vaccination with Pandemic influenza vaccine H5N1 AstraZeneca unless your doctor, nurse or pharmacist tells you otherwise. This is because of the risk of Reye's syndrome, a very rare but serious disease that can affect the brain and liver.
- **It is recommended that Pandemic influenza vaccine H5N1 AstraZeneca is not given** at the same time as influenza-specific **antiviral medicines** such as *oseltamivir* and *zanamivir*. This is because the vaccine may work less effectively.

Your doctor, nurse or pharmacist will decide if Pandemic influenza vaccine H5N1 AstraZeneca can be given at the same time as other vaccines.

Pregnancy and breast-feeding
- If you are **pregnant**, think you may be pregnant, or plan to become pregnant soon, **tell your doctor, nurse or pharmacist before vaccination**. He or she will decide if Pandemic influenza vaccine H5N1 AstraZeneca is suitable for you.
- Pandemic influenza vaccine H5N1 AstraZeneca is **not recommended** for **breast-feeding** women.

Driving and using machines
- Pandemic influenza vaccine H5N1 AstraZeneca has no or negligible influence on the ability to drive and use machines.

3. How Pandemic influenza vaccine H5N1 AstraZeneca is given

Pandemic influenza vaccine H5N1 AstraZeneca will be administered under the supervision of a doctor, nurse or pharmacist.

Pandemic influenza vaccine H5N1 AstraZeneca must only be used as a nasal spray.

Pandemic influenza vaccine H5N1 AstraZeneca must not be injected.

Pandemic influenza vaccine H5N1 AstraZeneca will be given as a spray in each nostril. You can breathe normally while you are given Pandemic influenza vaccine H5N1 AstraZeneca. You do not need to actively inhale or sniff.

Dosage
The recommended dose for children and adolescents is 0.2 ml Pandemic influenza vaccine H5N1 AstraZeneca, administered as 0.1 ml in each nostril. **All children** will receive a second, follow-up dose after an interval of at least 4 weeks.

If you have any further questions on this vaccine, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. In clinical studies with the vaccine, most side effects were mild in nature and short-term.

Ask your doctor, nurse or pharmacist if you want more information about possible side effects from Pandemic influenza vaccine H5N1 AstraZeneca.

Some side effects may be serious:

Very rare
(may affect up to 1 in 10,000 people):
- severe allergic reaction: signs of a severe allergic reaction may include shortness of breath and swelling of the face or tongue.

Tell your doctor straightaway or seek urgent medical care if you experience any of the effects above.

In clinical studies with adults who received Pandemic influenza vaccine H5N1 AstraZeneca, the most common side effects were headache and upper respiratory tract infection (inflammation of the nose, throat and sinuses).

Other possible side effects of Pandemic influenza vaccine H5N1 AstraZeneca in children and adolescents:

Very common
(may affect more than 1 in 10 people):
- runny or stuffy nose
- reduced appetite
- weakness

Common
(may affect up to 1 in 10 people):
- fever
- muscle aches
- headache

Uncommon
(may affect up to 1 in 100 people):
- rash
- nose bleed
- allergic reactions

Reporting of side effects
If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Pandemic influenza vaccine H5N1 AstraZeneca

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the applicator label after the letters EXP.

Store in a refrigerator (2°C to 8°C). Do not freeze.

Keep the nasal applicator in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Pandemic influenza vaccine H5N1 AstraZeneca contains

The active substance is:
Reassortant influenza virus* (live attenuated) of the following strain**:

A/Vietnam/1203/2004 (H5N1) strain
(A/Vietnam/1203/2004, MEDI 0141000136) $10^{7.0\pm0.5}$ FFU***

.....per 0.2 ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks.
** produced in VERO cells by reverse genetic technology. This product contains a genetically modified organism (GMO).
*** fluorescent focus units

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

The other ingredients are sucrose, dipotassium phosphate, potassium dihydrogen phosphate, gelatin (porcine, Type A), arginine hydrochloride, monosodium glutamate monohydrate and water for injections.

What Pandemic influenza vaccine H5N1 AstraZeneca looks like and contents of the pack

This vaccine is presented as a nasal spray suspension in a single-use nasal applicator (0.2 ml) in a pack size of 10.

The suspension is colourless to pale yellow, clear to slightly cloudy. Small white particles may be present.

Marketing Authorisation Holder
AstraZeneca AB
SE-151 85
Södertälje
Sweden

Manufacturer
AstraZeneca Nijmegen B.V.,
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

MedImmune, UK Limited
Plot 6, Renaissance Way
Boulevard Industry Park
Speke
Liverpool L24 9JW
United Kingdom

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

België/Belgique/Belgien
AstraZeneca S.A./N.V.
Tel: +32 2 370 48 11

България
АстраЗенека България ЕООД
Тел: +359 24455000

Česká republika
AstraZeneca Czech Republic s.r.o.
Tel: +420 222 807 111

Danmark
AstraZeneca A/S
Tlf.: +45 43 66 64 62

Deutschland
AstraZeneca GmbH
Tel: +49 40 809034100

Eesti
AstraZeneca
Tel: +372 6549 600

Lietuva
UAB ,AstraZeneca Lietuva
Tel: +370 5 2660550

Luxembourg/Luxemburg
AstraZeneca S.A./N.V.
Tél/Tel: +32 2 370 48 11

Magyarország
AstraZeneca Kft.
Tel.: +36 1 883 6500

Malta
Associated Drug Co. Ltd
Tel: +356 2277 8000

Nederland
AstraZeneca BV
Tel: +31 85 808 9900

Norge
AstraZeneca AS
Tlf: +47 21 00 64 00

Ελλάδα
AstraZeneca A.E.
Τηλ: +30 2-10 6871500

España
AstraZeneca Farmacéutica Spain, S.A.
Tel: +34 91 301 91 00

France
AstraZeneca
Tél: +33 1 41 29 40 00

Hrvatska
AstraZeneca d.o.o.
Tel: +385 1 4628 000

Ireland
AstraZeneca Pharmaceuticals (Ireland) Ltd
Tel: +353 1609 7100

Ísland
Vistor hf.
Sími: +354 535 7000

Italia
AstraZeneca S.p.A.
Tel: +39 02 00704500

Κύπρος
Αλέκτωρ Φαρμακευτική Λτδ
Τηλ: +357 22490305

Latvija
SIA AstraZeneca Latvija
Tel: +371 67377100

Österreich
AstraZeneca Österreich GmbH
Tel: +43 1 711 31 0

Polska
AstraZeneca Pharma Poland Sp. z o.o.
Tel.: +48 22 245 73 00

Portugal
AstraZeneca Produtos Farmacêuticos, Lda.
Tel: +351 21 434 61 00

România
AstraZeneca Pharma SRL
Tel: +40 21 317 60 41

Slovenija
AstraZeneca UK Limited
Tel: +386 1 51 35 600

Slovenská republika
AstraZeneca AB, o.z.
Tel: +421 2 5737 7777

Suomi/Finland
AstraZeneca Oy
Puh/Tel: +358 10 23 010

Sverige
AstraZeneca AB
Tel: +46 8 553 26 000

This leaflet was last revised in {MM/YYYY}

This medicine has been given "conditional approval". This means that there is more evidence to come about this medicine. The European Medicines Agency will review new information on this medicines at least every year and this leaflet will be updated as necessary.

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

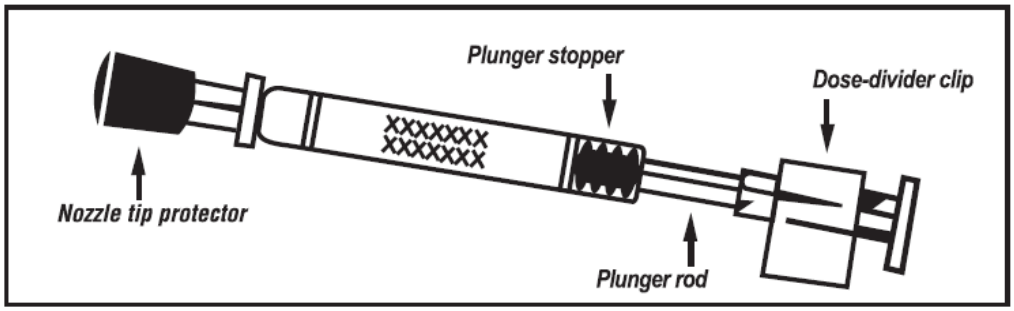
Instructions for healthcare professionals

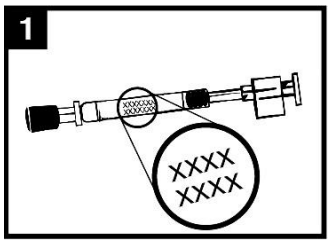
The following information is intended for healthcare professionals only:

Pandemic influenza vaccine H5N1 AstraZeneca is for nasal use only.

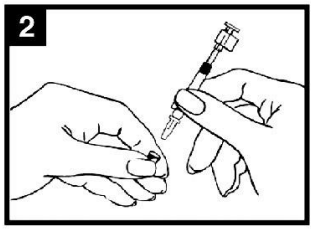
- **Do not use with a needle.** Do not inject.

- Do not use Pandemic influenza vaccine H5N1 AstraZeneca if the expiry date has passed or the sprayer appears damaged, for example, if the plunger is loose or displaced from the sprayer or if there are any signs of leakage.
- Check the appearance of the vaccine before administration. The suspension should be colourless to pale yellow, clear to opalescent. Small white particles may be present.
- Pandemic influenza vaccine H5N1 AstraZeneca is administered as a divided dose in both nostrils as described below. (See also *How Pandemic influenza vaccine H5N1 AstraZeneca is given,* in section 3).
- After administering half of the dose in one nostril, administer the other half of the dose in the other nostril immediately or shortly thereafter.
- The patient can breathe normally while the vaccine is being administered – there is no need to actively inhale or sniff.

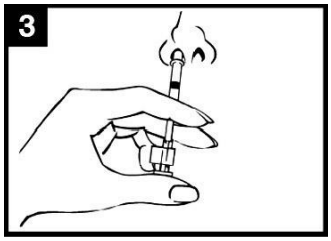




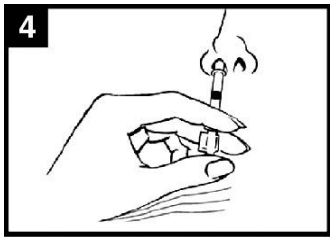
Check expiry date
Product must not be used after date on applicator label.



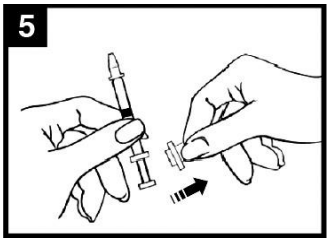
Prepare the applicator
Remove rubber tip protector. Do not remove dose-divider clip at the other end of the applicator.



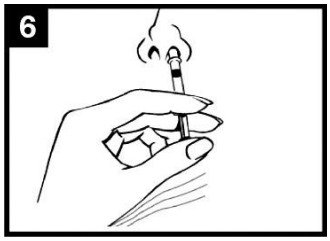
Position the applicator
With the patient in an upright position, place the tip just inside the nostril to ensure Pandemic influenza vaccine H5N1 AstraZeneca is delivered into the nose.



Depress the plunger
With a single motion, depress plunger **as rapidly as possible** until the dose-divider clip prevents you from going further.



Remove dose-divider clip
For administration in the other nostril, pinch and remove the dose-divider clip from plunger.



Spray in other nostril
Place the tip just **inside the other nostril** and with a single motion, depress plunger **as rapidly as possible** to deliver remaining vaccine.

See section 5 for advice on storage and disposal.