This information was recommended by the CHMP on 24 September 2009. It has been sent to the European Commission for the adoption of a formal decision applicable in all European Union Member States.

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Focetria suspension for injection in pre-filled syringe
Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain:

A/California/7/2009 (H1N1)v like strain (X-179A)	7.5 micrograms** per 0.5 ml dose

* propagated in eggs
** expressed in microgram haemagglutinin.

Adjuvant MF59C.1 containing:

squalene	9.75 milligrams
polysorbate 80	1.175 milligrams
sorbitan trioleate	1.175 milligrams

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

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.
Milky-white liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

This pandemic influenza vaccine H1N1 has been authorised based on data obtained with a version containing H5N1 antigen supplemented with data obtained with the vaccine containing H1N1 antigen.
The Clinical Particulars section will be updated in accordance with emerging additional data.

There is currently no clinical experience with Focetria (H1N1) in adults, including the elderly, children or adolescents. The decision to use Focetria (H1N1) in each age group defined below should take into account the extent of the clinical data available with a version of the vaccine containing H5N1 antigen and the disease characteristics of the current influenza pandemic.

The dose recommendations are based on the:

- safety and immunogenicity data available on the administration of the MF59C.1 adjuvanted vaccine containing 7.5 ug HA derived from A/Vietnam/1194/2004 (H5N1) at 0 and 21 days to adults, including the elderly, and children between 6 months and 17 years of age.

See sections 4.8 and 5.1.

Posology:

Adults and elderly
One dose of 0.5 ml at an elected date.
A second dose of vaccine should be given after an interval of at least three weeks.

Children and adolescents 6 months to 17 years of age
One dose of 0.5 ml at an elected date.
A second dose of vaccine should be given after an interval of at least three weeks.

Children aged less than 6 months
Vaccination is not currently recommended in this age group.

It is recommended that subjects who receive a first dose of Focetria, complete the vaccination course with Focetria (see section 4.4).

For further information, see sections 4.8 and 5.1.

Method of administration
Immunisation should be carried out by intramuscular injection preferably into the deltoid muscle or anterolateral thigh (depending on the muscle mass).

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to any of the constituents or trace residues (egg and chicken proteins, ovalbumin, kanamycin and neomycin sulphate, formaldehyde and cetyltrimethylammonium bromide (CTAB)) of this vaccine. If vaccination is considered to be necessary, facilities for resuscitation should be immediately available in case of need.

See section 4.4 for Special warnings and special precautions for use.

4.4 Special warnings and precautions for use

Caution is needed when administrating this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients and to residues (eggs and chicken protein, ovalbumin, kanamycin and neomycin sulphate, formaldehyde and cetyltrimethylammonium bromide (CTAB)).

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.

Focetria should under no circumstances be administered intravascularly or subcutaneously.

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

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

There are no safety, immunogenicity or efficacy data to support interchangeability of Focetria with other H1N1 pandemic vaccines.

4.5 Interaction with other medicinal products and other forms of interaction

Data on co-administration of subunit not adjuvanted influenza seasonal and H5N1 vaccines in adults did not suggest any interference in the immune response to seasonal or to H5N1 antigens. There were no differences

in serious adverse events (SAEs) between groups, and all SAEs were unrelated. These data suggest that Focetria can be given at the same time as non adjuvanted subunit seasonal influenza vaccines.
There are no data on co-administration of Focetria with other vaccines.
However, if co-administration with another vaccine is considered, 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

There are currently no data available on the use of Focetria in pregnancy. Data from pregnant women vaccinated with different inactivated non-adjuvanted seasonal vaccines do not suggest malformations or fetal or neonatal toxicity.

Animal studies with Focetria do not indicate reproductive toxicity (see section 5.3).
The use of Focetria may be considered during pregnancy if this is thought to be necessary, taking into account official recommendations.
Focetria may be used in lactating women..

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 use machines.

4.8 Undesirable effects

- Clinical trials

Adult and Elderly
In clinical trials with different formulations (H5N3, H9N2 and H5N1) 542 subjects were exposed to the mock-up vaccine. Of theses subjects, 464 subjects received the mock-up vaccine (A/H5N1).
From the clinical trials with the pandemic vaccine, most of the reactions were mild in nature, of short duration and qualitatively similar to those induced by conventional seasonal influenza vaccines. It is widely accepted that the adjuvant effect leading to increased immunogenicity is associated with a slightly higher frequency of local reactions (mostly mild pain) compared with conventional, nonadjuvanted influenza vaccines. There were fewer reactions after the second vaccination compared with the first.

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

The incidence of symptoms observed in subjects over 60 years of age was lower as compared to the 18-60 years old population.

Adverse reactions reported are listed according to the following frequency:
Very common (≥1/10),
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100),
Rare (≥1/10,000 to <1/1,000),
Very rare (<1/10,000).

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

Nervous system disorders
Common: headache

Skin and subcutaneous tissue disorders
Common: sweating

Muscoskeletal, connective tissue and bone disorders
Common: arthralgia and myalgia

General disorders and administration site conditions
Common: injection site redness, injection site swelling, injection site induration, injection site ecchymosis and injection site pain, fever, malaise, fatigue and shivering

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

Children and adolescents 6 months to 17 years of age
A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 471 children from 6 months to 17 years of age. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) at the dosage of 7.5 µg hemagglutinin [HA]/dose with MF59C.1 adjuvant were administered three weeks apart. The effect of the administration of a booster dose 12 months following the second dose has also been evaluated.

Local and systemic reactogenicity was monitored for the week following vaccine administration. Local reactions were more frequent at subsequent administrations following the first one, at any age.
Most systemic reactions were experienced within 3 days following vaccination and were transient and mild of moderate severity.
In these age groups, the per-dose frequency of reactions was higher than the one reported for adults and elderly. A higher frequency of fever >39.0°C was also observed.
Systemic adverse events reported very commonly in the 6 months-35 months of age group per dose were irritability, unusual crying, sleepiness, diarrhoea and change in eat habits. In children very common systemic events included headache, fatigue. Among the adolescents the very common events were: malaise, myalgia, headache, fatigue, sweating, nausea, chills.

Percentages of subjects with solicited and unsolicited reactions are provided below:

	Injection 1	**Injection 2**
Toddlers (6 to 35 months)	**N=145**	**N=138**
Local	47%	46%
Systemic	59%	51%
Fever ≥ 38°C/≥ 39°C/≥ 40° C	7% / 1% / 0%	12% / 3% / 0%
Any other AE	54%	49%
Children (3 to 9 years of age)	**N=96**	**N=93**
Local	66%	58%
Systemic	32%	33%
Fever ≥ 38°C/≥ 39°C/≥ 40° C	4% / 1% / 0%	2% / 0% / 0%
Any other AE	36%	31%
Adolescents (10 to 17 years of age)	**N=93**	**N=91**
Local	81%	70%
Systemic	69%	52%
Fever ≥ 38°C/≥ 39°C/≥ 40°C	0% / 0% / 0%	1% / 0% / 0%
Any other AE	30%	27%

- Post-marketing surveillance

From Post-marketing surveillance with interpandemic trivalent vaccines in all age groups and with adjuvanted interpandemic trivalent vaccines with the similar composition of Focetria (surface antigen,

inactivated, adjuvanted with MF59C.1), licensed for use in elderly subjects above 65 years of age, the following adverse events have been reported:

Uncommon:
Generalised skin reactions including pruritus, urticaria or non-specific rash.

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

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

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC Code: J07BB02

This medicinal product has been authorised under "exceptional Circumstances".
The European Medicines Agency (EMEA) will regularly review any new information which may become available and this SPC will be updated as necessary.

This section describes the clinical experience with the mock-up vaccines following a two-dose administration. After the second dose, an SRH antibody area equal or superior than 25 mm^2 is generally obtained within 3 weeks.

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 a 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.

A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 486 healthy adult volunteers. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) (7.5 µg hemagglutinin [HA]/dose) with MF59C.1 adjuvant were administered three weeks apart.

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in the adults measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	41% (95% CI: 33-49)	86% (95% CI: 79-91)
Seroconversion rate	39% (95% CI: 31-47)	85% (95% CI: 79-91)
Seroconversion factor	2.42 (2.02-2.89)	7.85 (6.7-9.2)

* measured by SRH assay ≥ 25 mm
** geometric mean ratios of SRH

The seroprotection rate*, seroconversion rate* and the seroconversion factor ** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in subjects aged over 60 measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	53% (95% CI: 42-64)	81% (95% CI: 71-89)
Seroconversion rate	45% (95% CI: 34-56)	71% (95% CI: 60-81)
Seroconversion factor	2.85 (2.22-3.66)	5.02 (3.91-6.45)

* measured by SRH assay ≥ 25 mm
** geometric mean ratios of SRH

Limited data on the persistence of antibodies for the mock-up vaccines is available.

Cross-reactivity of highly pathogenic variants of A/Vietnam/1194/2004 (H5N1) in subjects 18 years and above.
Immunogenicity analyses were carried out for influenza A/H5N1/turkey/Turkey/05 (NIBRG23; clade 2.2) with HI, SRH, and MN and for influenza A/H5N1/Indonesia (clade 2.1) with HI and MN, on sera collected 3 weeks after the second vaccination (day 43) and 3 weeks after the booster vaccination (day 223).
In both age groups the responses to the heterologous strains highly increased after booster vaccination with the mock-up vaccine by all assays used.

- Studies in children

A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 471 children from 6 months to 17 years of age. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) at the dosage of 7.5 µg hemagglutinin [HA]/dose with MF59C.1 adjuvant were administered three weeks apart.

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody antibody to H5N1 A/Vietnam/1194/2004 in the toddlers aged from 6 to 35 months measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	47% (CI: 38-55)	100% (CI: 97-100)
Seroconversion rate	44% (CI: 36-53)	98% (CI: 95-100)
Seroconversion factor	2.67 (2.24-3.18)	16 (14-18)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody antibody to H5N1 A/Vietnam/1194/2004 in the children aged from 3 to 8 years measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	54% (CI: 44-65)	100% (CI: 96-100)
Seroconversion rate	56% (CI: 45-66)	100% (CI: 96-100)
Seroconversion factor	3.34 (2.74-4.06)	15 (13-17)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody antibody to H5N1 A/Vietnam/1194/2004 in the adolescent aged from 9 to 17 years measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose

Seroprotection rate	59%(CI: 48-69)	100% (CI: 96-100)
Seroconversion rate	57% (CI: 46-67)	99% (CI: 94-100)
Seroconversion factor	3.87 (3.25-4.61)	14 (12-16)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

- Supportive Studies

In two dose finding studies 78 adults received an adjuvanted mock-up vaccine (H5N3 or H9N2).
Two doses of vaccine with H5N3 (A/Duck/Singapore/97) strain at 3 different dosages (7.5, 15 and 30 µg HA/dose) were administered three weeks apart.
Serum samples were tested against the original H5N3 and also a number of H5N1 isolates.
Serologic responses obtained with the SRH assay showed that 100% of subjects achieved seroprotection and 100% seroconverted after two 7.5 µg injections. The adjuvanted vaccine was also found to induce antibodies that cross-protected against the H5N1 strains isolated in 2003 and 2004, which exhibit some antigenic drift compared to the original strains.

Two doses of vaccine containing H9N2 (A/chicken/Hong Kong/G9/97) strain at 4 different dosages (3.75, 7.5, 15 and 30 µg HA/dose), were administered four weeks apart. Serologic responses obtained with the Hemagglutination Inhibition (HI) assay showed that 92% of subjects achieved seroprotection and 75% seroconverted after two 7.5 µg injections.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data obtained with the mock-up vaccine using a H5N1 vaccine strain and with vaccine containing MF59C.1 adjuvant reveal no special hazard for humans based on conventional studies of efficacy, repeated dose toxicity, and reproductive and developmental toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,
Potassium chloride,
Potassium dihydrogen phosphate,
Disodium phosphate dihydrate,
Magnesium chloride hexahydrate,
Calcium chloride dihydrate,
Sodium citrate,
Citric acid,
Water for injections.

For the adjuvant, 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

1 year.

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

0.5 ml in pre-filled syringe (type I glass) with plunger-stopper (bromo-butyl rubber). Packs of 1 and 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The vaccine should be allowed to reach room temperature before use. Gently shake before use.
Any unused vaccine or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Vaccines and Diagnostics S.r.l. - Via Fiorentina, 1 – Siena, Italy.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/385/001
EU/1/07/385/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 May 2007

10. DATE OF REVISION OF THE TEXT

09/2009

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

1. NAME OF THE MEDICINAL PRODUCT

Focetria suspension for injection in multidose container
Pandemic influenza vaccine (surface antigen, inactivated, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain:

A/California/7/2009 (H1N1)v like strain (X-179A)	7.5 micrograms ** per 0.5 ml dose

* propagated in eggs
** expressed in microgram haemagglutinin.

Adjuvant MF59C.1 containing:	
squalene	9.75 milligrams
polysorbate 80	1.175 milligrams
sorbitan trioleate	1.175 milligrams
Excipients:	
thiomersal	0.05 milligrams

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

This is a multidose container.
See section 6.5 for the number of doses per vial.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Milky-white liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

This pandemic influenza vaccine H1N1 has been authorised based on data obtained with a version containing H5N1 antigen supplemented with data obtained with the vaccine containing H1N1 antigen.
The Clinical Particulars section will be updated in accordance with emerging additional data.

There is currently no clinical experience with Focetria (H1N1) in adults, including the elderly, children or adolescents.

The decision to use Focetria (H1N1) in each age group defined below should take into account the extent of the clinical data available with a version of the vaccine containing H5N1 antigen and the disease characteristics of the current influenza pandemic.

The dose recommendations are based on the:

- safety and immunogenicity data available on the administration of the MF59C.1 adjuvanted vaccine containing 7.5 ug HA derived from A/Vietnam/1194/2004 (H5N1) at 0 and 21 days to adults, including the elderly, and children between 6 months and 17 years of age.

See sections 4.8 and 5.1.

Posology:

Adults and elderly
One dose of 0.5 ml at an elected date.
A second dose of vaccine should be given after an interval of at least three weeks.

Children and adolescents 6 months to 17 years of age
One dose of 0.5 ml at an elected date.
A second dose of vaccine should be given after an interval of at least three weeks.

Children aged less than 6 months
Vaccination is not currently recommended in this age group.

For further information, see sections 4.8 and 5.1.

Method of administration
Immunisation should be carried out by intramuscular injection preferably into the deltoid muscle or anterolateral thigh (depending on the muscle mass).

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to any of the constituents or trace residues (egg and chicken proteins, ovalbumin, kanamycin and neomycin sulphate, formaldehyde and cetyltrimethylammonium bromide (CTAB)) of this vaccine. If vaccination is considered to be necessary, facilities for resuscitation should be immediately available in case of need.
See section 4.4. for Special warnings and special precautions for use.

4.4 Special warnings and precautions for use

Caution is needed when administrating this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients, to thiomersal and to residues (eggs and chicken protein, ovalbumin, kanamycin and neomycin sulphate, formaldehyde and cetyltrimethylammonium bromide (CTAB)).

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.

Focetria should under no circumstances be administered intravascularly or subcutaneously.

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

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

There are no safety, immunogenicity or efficacy data to support interchangeability of Focetria with other H1N1 pandemic vaccines.

4.5 Interaction with other medicinal products and other forms of interaction

Data on co-administration of subunit influenza not adjuvanted seasonal and H5N1 vaccines in adults did not suggest any interference in the immune response to seasonal or to H5N1 antigens. There were no differences in serious adverse events (SAEs) between groups, and all SAEs were unrelated. This data suggest that Focetria can be given at the same time as non adjuvanted subunit seasonal influenza vaccines. There are no data on co-administration of Focetria with 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 have been observed. In such cases, the Western Blot method is negative. These transitory false-positive results may due to IgM production in response to the vaccine.

4.6 Pregnancy and lactation

There are currently no data available on the use of Focetria in pregnancy. Data from pregnant women vaccinated with different inactivated non-adjuvanted seasonal vaccines do not suggest malformations or fetal or neonatal toxicity.

Animal studies with Focetria do not indicate reproductive toxicity (see section 5.3).
The use of Focetria may be considered during pregnancy if this is thought to be necessary, taking into account official recommendations.

Focetria may be used in lactacting women.

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 use machines.

4.8 Undesirable effects

- Clinical trials

Adults and elderly
In clinical trials with different formulations (H5N3, H9N2 and H5N1) 542 subjects were exposed to the candidate vaccine. Of theses subjects, 464 subjects received the mock-up vaccine (A/H5N1).
From the clinical trials with the pandemic vaccine, most of the reactions were mild in nature, of short duration and qualitatively similar to those induced by conventional seasonal influenza vaccines. It is widely accepted that the adjuvant effect leading to increased immunogenicity is associated with a slightly higher frequency of local reactions (mostly mild pain) compared with conventional, nonadjuvanted influenza vaccines. There were fewer reactions after the second vaccination compared with the first.

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

The incidence of symptoms observed in subjects over 60 years of age was lower as compared to the 18-60 years old population.

Adverse reactions reported are listed according to the following frequency:
Very common (≥1/10),

Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100),
Rare (≥1/10,000 to <1/1,000),
Very rare (<1/10,000).

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

Nervous system disorders
Common: headache

Skin and subcutaneous tissue disorders
Common: sweating

Muscoskeletal, connective tissue and bone disorders
Common: arthralgia and myalgia

General disorders and administration site conditions
Common: injection site redness, injection site swelling, injection site induration, injection site ecchymosis and injection site pain, fever, malaise, fatigue and shivering

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

Children and adolescents 6 months to 17 years of age
A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 471 children from 6 months to 17 years of age. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) at the dosage of 7.5 µg hemagglutinin [HA]/dose with MF59C.1 adjuvant were administered three weeks apart. The effect of the administration of a booster dose 12 months following the second dose has also been evaluated.

Local and systemic reactogenicity was monitored for the week following vaccine administration. Local reactions were more frequent at subsequent administrations following the first one, at any age.
Most systemic reactions were experienced within 3 days following vaccination and were transient and mild of moderate severity.
In these age groups, the per-dose frequency of reactions was higher than the one reported for adults and elderly. A higher frequency of fever >39.0°C was also observed.
Systemic adverse events reported very commonly in the 6 months-35 months of age group per dose were irritability, unusual crying, sleepiness, diarrhea and change in eat habits. In children very common systemic events included headache, fatigue. Among the adolescents the very common events were: malaise, myalgia, headache, fatigue, sweating, nausea, chills.

Percentages of subjects with solicited and unsolicited reactions are provided below:

	Injection 1	**Injection 2**
Toddlers (6-35 months months)	**N=145**	**N=138**
Local	47%	46%
Systemic	59%	51%
Fever ≥ 38°C/≥ 39°C/≥ 40° C	7% / 1% / 0%	12% / 3% / 0%
Any other AE	54%	49%
Children (3 – 9 years of age)	**N=96**	**N=93**
Local	66%	58%
Systemic	32%	33%
Fever ≥ 38°C/≥ 39°C/≥ 40° C	4% / 1% / 0%	2% / 0% / 0%
Any other AE	36%	31%
Adolescents (10 -17 years of age)	**N=93**	**N=91**
Local	81%	70%
Systemic	69%	52%

Fever ≥ 38°C/≥ 39°C/≥ 40°C	0% / 0% / 0%	1% / 0% / 0%
Any other AE	30%	27%

- Post-marketing surveillance

From Post-marketing surveillance with interpandemic trivalent vaccines in all age groups and with adjuvanted interpandemic trivalent vaccines with the similar composition of Focetria (surface antigen, inactivated, adjuvanted with MF59C.1), licensed for use in elderly subjects above 65 years of age, the following adverse events have been reported:

Uncommon:
Generalised skin reactions including pruritus, urticaria or non-specific rash.

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

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

Thiomersal:
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 vaccine, ATC Code: J07BB02

This medicinal product has been authorised under "exceptional Circumstances".
The European Medicines Agency (EMEA) will regularly review any new information which may become available and this SPC will be updated as necessary.

This section describes the clinical experience with the mock-up vaccines following a two-dose administration. After the second dose, an SRH antibody area equal or superion than 25 mm^2 is generally obtained within 3 weeks.

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 a 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.

A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 486 healthy adult volunteers. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) (7.5 µg hemagglutinin [HA]/dose) with MF59C.1 adjuvant were administered three weeks apart.

The seroprotection rate* seroconversion rate* and the seroconversion factor ** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in the adults measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	41% (95% CI: 33-49)	86% (95% CI: 79-91)
Seroconversion rate	39% (95% CI: 31-47)	85% (95% CI: 79-91)
Seroconversion factor	2.42 (2.02-2.89)	7.85 (6.7-9.2)

* measured by SRH assay ≥ 25 mm
** geometric mean ratios of SRH

The seroprotection rate* seroconversion rate* and the seroconversion factor ** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in subjects aged over 60 measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	53% (95% CI: 42-64)	81% (95% CI: 71-89)
Seroconversion rate	45% (95% CI: 34-56)	71% (95% CI: 60-81)
Seroconversion factor	2.85 (2.22-3.66)	5.02 (3.91-6.45)

* measured by SRH assay ≥ 25 mm
** geometric mean ratios of SRH

Limited data on the persistence of antibodies for the mock-up vaccines is available.

Cross-reactivity of highly pathogenic variants of A/Vietnam/1194/2004 (H5N1) in subjects 18 years and above.
Immunogenicity analyses were carried out for influenza A/H5N1/turkey/Turkey/05 (NIBRG23; clade 2.2) with HI, SRH, and MN and for influenza A/H5N1/Indonesia (clade 2.1) with HI and MN, on sera collected 3 weeks after the second vaccination (day 43) and 3 weeks after the booster vaccination (day 223).
In both age groups the responses to the heterologous strains highly increased after booster vaccination with the mock-up vaccine by all assays used.

- Studies in children

A clinical trial was conducted with a H5N1 vaccine combined with MF59C.1 adjuvant in 471 children from 6 months to 17 years of age. Two doses of vaccine containing H5N1 (A/Vietnam/1194/2004) at the dosage of 7.5 µg hemagglutinin [HA]/dose with MF59C.1 adjuvant were administered three weeks apart.

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in the toddlers aged from 6 to 35 months measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	47% (CI: 38-55)	100% (CI: 97-100)
Seroconversion rate	44% (CI: 36-53)	98% (CI: 95-100)
Seroconversion factor	2.67 (2.24-3.18)	16 (14-18)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in the children aged from 3 to 8 years measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	54% (CI: 44-65)	100% (CI: 96-100)

Seroconversion rate	56% (CI: 45-66)	100% (CI: 96-100)
Seroconversion factor	3.34 (2.74-4.06)	15 (13-17)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

The seroprotection rate*, seroconversion rate* and the seroconversion factor** for anti-HA antibody to H5N1 A/Vietnam/1194/2004 in the adolescent aged from 9 to 17 years measured by SRH were as follows:

anti-HA antibody	21 days after 1st dose	21 days after 2nd dose
Seroprotection rate	59%(CI: 48-69)	100% (CI: 96-100)
Seroconversion rate	57% (CI: 46-67)	99% (CI: 94-100)
Seroconversion factor	3.87 (3.25-4.61)	14 (12-16)

* measured by SRH assay ≥ 25 mm^2
** geometric mean ratios of SRH

- Supportive Studies

In two dose finding studies 78 adults received an adjuvanted mock-up vaccine (H5N3 or H9N2).
Two doses of vaccine with H5N3 (A/Duck/Singapore/97) strain at 3 different dosages (7.5, 15 and 30 µg HA/dose) were administered three weeks apart.
Serum samples were tested against the original H5N3 and also a number of H5N1 isolates.
Serologic responses obtained with the SRH assay showed that 100% of subjects achieved seroprotection and 100% seroconverted after two 7.5 µg injections. The adjuvanted vaccine was also found to induce antibodies that cross-protected against the H5N1 strains isolated in 2003 and 2004, which exhibit some antigenic drift compared to the original strains.

Two doses of vaccine containing H9N2 (A/chicken/Hong Kong/G9/97) strain at 4 different dosages (3.75, 7.5, 15 and 30 µg HA/dose), were administered four weeks apart. Serologic responses obtained with the Hemagglutination Inhibition (HI) assay showed that 92% of subjects achieved seroprotection and 75% seroconverted after two 7.5 µg injections.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data obtained with the mock-up vaccine using a H5N1 vaccine strain and with vaccine containing MF59C.1 adjuvant reveal no special hazard for humans based on conventional studies of efficacy, repeated dose toxicity, and reproductive and developmental toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,
Potassium chloride,
Potassium dihydrogen phosphate,
Disodium phosphate dihydrate,
Magnesium chloride hexahydrate,
Calcium chloride dihydrate,
Sodium citrate,

Citric acid,
Thiomersal,
Water for injections.

For the adjuvant, 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

1 year.

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

5.0 ml in 10-dose vial (type I glass) with stopper (halo-butyl rubber). Packs of 10.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Gently shake the multidose vial each time before withdrawing a dose (0.5 ml) of the vaccine into a syringe. Prior to administration, the withdrawn vaccine should be allowed reach room temperature.

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

7. MARKETING AUTHORISATION HOLDER

Novartis Vaccines and Diagnostics S.r.l. - Via Fiorentina, 1 – Siena, Italy.

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/385/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 May 2007

10. DATE OF REVISION OF THE TEXT

09/2009

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

ANNEX II

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

Name and address of the manufacturers of the biological active substance

(Manufacturer responsible for monovalent pooled harvests, before final filtration):
Novartis Vaccines and Diagnostics S.r.l.
Via Fiorentina, 1 – 53100 Siena
Italy

(Manufacturer responsible for final filtration of monovalent pooled harvest):
Novartis Vaccines and Diagnostics S.r.l.
Loc. Bellaria – 53018 Rosia – Sociville (SI)
Italy

Name and address of the manufacturer(s) responsible for batch release

Novartis Vaccines and Diagnostics S.r.l.
Loc. Bellaria – 53018 Rosia – Sociville (SI)
Italy

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.

Focetria 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 Focetria takes due account of the officially declared pandemic strain.

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

- The MAH shall agree with Member States to measures facilitating the identification and traceability of the A/H1N1 pandemic vaccine administered to each patient, in order to minimise medication errors and aid patients and health care professionals to report adverse reactions. This may include the provision by the MAH of stickers with invented name and batch number with each pack of the vaccine.

- The MAH shall agree with Member States on mechanisms allowing patients and health care professionals to have continuous access to updated information regarding Focetria.

- The MAH shall agree with Member States on reasonable measures for the provision of a targeted communication to healthcare professionals which should address the following:

    - The correct way to prepare the vaccine prior to administration.

    - Adverse events to be prioritised for reporting, i.e. fatal and life-threatening adverse reactions, unexpected severe adverse reactions, adverse events of special interest (AESI).

- The minimal data elements to be transmitted in individual case safety reports in order to facilitate the evaluation and the identification of the vaccine administered to each subject, including the invented name, the vaccine manufacturer and the batch number.

- If a specific notification system has been put in place, how to report adverse reactions.

- **OTHER CONDITIONS**

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.

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, as described in version 1.3 (dated 18 September 2009) presented in Module 1.8.1 of the marketing authorisation application, is in place and functioning before the product is placed on the market and for as long as the marketed product remains in use.

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 benefit-risk balance in a pandemic. Prompt analysis of cumulative safety information, in light of the extent of exposure, will be crucial for regulatory decisions and protection of the population to be vaccinated. The MAH shall submit on a monthly basis a simplified periodic safety update report with the timelines, format and content as defined in the CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine (EMEA/359381/2009) and any subsequent update.

Risk Management plan

The MAH commits to performing the studies and additional pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in version RMPv1.3 (dated 18 September 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.

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 continuous reassessment of the benefit/risk profile.

Clinical	The MAH commits to provide abridged reports for the following studies performed in adults: Safety and immunogenicity data: Study V111_02: -post day 1 -post day 2	 12 October 2009 07 December 2009

	Study V111_04: -post day 1 -post day 2	 15 November 2009 11 January 2010
Clinical	The MAH commits to provide abridged reports for the following study performed in children: Safety and immunogenicity data: Study V111_03 - post day 1 - post day 2	 01 December 2009 29 January 2010
Clinical	The MAH commits to submit the protocol and provide the results of the effectiveness studies carried out in accordance with the study protocols published by ECDC.	Protocol to be submitted on 15 October 2009. Results of studies to be provided within two weeks of availability.
Pharmacovigilance	The MAH will submit the protocol and the results of a prospective cohort safety study in at least 9,000 patients in different age groups, including immunocompromised subjects, in accordance with the protocol submitted with the Risk Management Plan. Observed-to-Expected analyses will be performed.	Protocol to be submitted by 15 October. Interim and final results will be submitted in accordance with the protocol.
Pharmacovigilance	The MAH commits to submit the details of the design and report the results of a study in a pregnancy registry.	Details to be submitted within one month of the Commission Decision granting the Variation. Results to be provided in the simplified PSUR.
Pharmacovigilance	The MAH commits to establish the mechanism to promptly investigate issues affecting the benefit-risk balance of the vaccine.	Agree with EMEA on design of additional studies for emerging benefit-risk evaluation within 1 month of the Commission Decision granting the Variation.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARDBOARD BOX FOR SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Focetria suspension for injection in pre-filled syringe
Pandemic Influenza Vaccine (surface antigen, inactivated, adjuvanted)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 ml) contains: Active Ingredients: Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in eggs, and adjuvanted with MF59C.1, of strain:

A/California/7/2009 (H1N1)v like strain (X-179A) 7.5 micrograms haemagglutinin

Adjuvant: MF59C.1 oil in water emulsion containing squalene, as the oil phase, stabilised with polysorbate 80 and sorbitan trioleate in a citrate buffer.

3. LIST OF EXCIPIENTS

Sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, sodium citrate, citric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

1 x single dose (0.5 ml) pre-filled syringe
10 x single dose (0.5 ml) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

To be administered intramuscularly into the deltoid muscle.

Warning: Do not inject intravascularly or subcutaneously.

Read the package leaflet before use.

The vaccine should be allowed to reach room temperature before use. Gently shake 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

8. EXPIRY DATE

EXP.:

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

Novartis Vaccines and Diagnostics S.r.l. - Via Fiorentina, 1 – Siena, Italy.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/385/001
EU/1/07/385/002

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

CARDBOARD BOX FOR 10-DOSE VIAL

1. NAME OF THE MEDICINAL PRODUCT

Focetria suspension for injection in multidose container
Pandemic Influenza Vaccine (surface antigen, inactivated, adjuvanted)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 ml) contains: Active Ingredients: Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in eggs, and adjuvanted with MF59C.1, of strain:

A/California/7/2009 (H1N1)v like strain (X-179A) 7.5 micrograms haemagglutinin

Adjuvant: MF59C.1 oil in water emulsion containing squalene, as the oil phase, stabilised with polysorbate 80 and sorbitan trioleate in a citrate buffer.

3. LIST OF EXCIPIENTS

Sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, sodium citrate, citric acid, thiomersal, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.
Vial
10 x 10 doses
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

To be administered intramuscularly into the deltoid muscle.

Warning: Do not inject intravascularly or subcutaneously.

Read the package leaflet before use.

The vaccine should be allowed to reach room temperature before use. Gently shake 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

8. EXPIRY DATE

EXP.:

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 requirements

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Vaccines and Diagnostics S.r.l. - Via Fiorentina, 1 – Siena, Italy.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/385/004

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

LABEL FOR SYRINGE

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

Focetria injection
Pandemic influenza vaccine
Intramuscular use

2. METHOD OF ADMINISTRATION

Shake before use.

3. EXPIRY DATE

EXP.:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

Store in a refrigerator.
Novartis V&D S.r.l.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL FOR 10-DOSE VIAL

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

Focetria injection
Pandemic Influenza Vaccine
Intramuscular use.

2. METHOD OF ADMINISTRATION

Gently shake before use.

3. EXPIRY DATE

EXP.:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Multidose vial (5 ml)

6. OTHER

Store in a refrigerator.
Novartis V&D S.r.l.

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Focetria suspension for injection
Pandemic Influenza Vaccine (H1N1) (surface antigen, inactivated, adjuvanted)

For the most up-to-date information please consult the website of the European Medicines Agency (EMEA): http://www.emea.europa.eu

Read all of this leaflet carefully before you receive this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. WHAT FOCETRIA IS AND WHAT IT IS USED FOR

Focetria is a vaccine to prevent pandemic influenza (flu).

Pandemic flu is a type of influenza that occurs every few decades and which spreads rapidly around the world. The symptoms of pandemic flu are similar to those of an ordinary flu but may be 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 ingredient in the vaccine can cause flu.

2. BEFORE YOU RECEIVE FOCETRIA

You should not receive Focetria:

- if you have previously had a sudden life-threatening allergic reaction to any ingredient of Focetria (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, kanamycin and neomycin sulphate (antibiotics) or cetyltrimethylammonium bromide (CTAB). 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.

If you are not sure, talk to your doctor or nurse before having this vaccine.

Take special care with Focetria:

- if you have had any allergic reaction other than a sudden life-threatening allergic reaction to any ingredient contained in the vaccine, to thiomersal (only for the multidose vial presentation), to egg and, chicken protein, ovalbumin, formaldehyde, kanamycin and neomycin sulphate (antibiotics) or cetyltrimethylammonium bromide (CTAB). (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 or nurse should advise whether you could still be vaccinated with Focetria,

- if you are having a blood test to look for evidence of infection with certain viruses. In the first few weeks after vaccination with Focetria the results of these tests may not be correct. Tell the doctor requesting these tests that you have recently been given Focetria.

In any of these cases, TELL YOUR DOCTOR OR NURSE, as vaccination may not be recommended, or may need to be delayed.

Taking other medicines

Please tell your doctor or nurse if you are taking or have recently taken any other medicines, including medicines obtained without a prescriptionor have recently been given any other vaccine.
Information suggest that Focetria can be given at the same time as a type of seasonal influenza vaccine called non-adjuvanted subunit vaccine.

There is no information on administration of the vaccine Focetria with any other vaccines other than seasonal vaccine. However, if this cannot be avoided, the vaccines should be injected into separate limbs. In such cases, you should be aware that the side effects may be more intense.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant, think you may be pregnant, plan to become pregnant. You should discuss with your doctor whether you should receive Focetria.
The vaccine may be used during 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 Focetria

This vaccine in a multi-dose vial contains thiomersal as a preservative and it is possible that you may experience an allergic reaction. Tell your doctor if you have any known allergies.
This medicinal 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 FOCETRIA IS GIVEN

Your doctor or nurse will administer the vaccine in accordance with official recommendations.
The vaccine will be injected into a muscle (usually in the upper arm).

Adults, including the elderly:
A dose (0.5 ml) of the vaccine will be given.
A second dose of vaccine should be given after an interval of at least three weeks.

Children and adolescents
If it is considered that you or your child needs to be vaccinated, you/he/she will receive one dose of 0.5 ml vaccine and a second dose of 0.5 ml at least three weeks later.

<u>Children aged less than 6 months of age</u>

Vaccination is currently not recommended in this age group.

When Focetria is given for the first dose, it is recommended that Focetria (and not another vaccine against H1N1) be given for the complete vaccination course.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Focetria can cause side effects, although not everybody gets them.
Allergic reactions may occur following vaccination, in rare cases leading to shock. Doctors are aware of this possibility and have emergency treatment available for use in such cases.

In the clinical studies with a similar vaccine, most side effects were mild in nature and short term. The side-effects are generally similar to those related to the seasonal flu vaccine.

The frequency of possible side effects listed below is defined using the following convention:
very common (affects more than 1 user in 10)
common (affects 1 to 10 users in 100)
uncommon (affects 1 to 10 users in 1,000)
rare (affects 1 to 10 users in 10,000)
very rare (affects less than 1 user in 10,000)

The side effects listed below have occurred with Focetria in clinical studies in adults, including the elderly:

Common:
Redness, swelling or pain at the site of injection, bruising or hardening of the skin at the injection site, fever, generally feeling unwell, tiredness, headache, increased sweating, shivering, flu like symptoms, aching muscles, joint pain.
These side effects usually disappear within 1-2 days without treatment. If they persist, CONSULT YOUR DOCTOR.

Side effects from clinical studies in children
A clinical study was conducted with a similar vaccine in children. General side effects reported very commonly in the 6 months-36 months of age group per dose were irritability, unusual crying, sleepiness, diarrhoea and change in eating habits. In children very common systemic events included headache, fatigue. Among the adolescents the very common events were: generally feeling unwell, pain, headache, fatigue, sweating, nausea and chills.

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

Uncommon:
Generalised skin reactions including urticaria (hives).

Rare:
Allergic reactions leading to a dangerous decrease of blood pressure, which, if untreated, may lead to shock. Doctors are aware of this possibility and have emergency treatment available for use in such cases, fits, severe stabbing or throbbing pain along one or more nerves, low blood platelet count which can result in bleeding or bruising

Very rare:
Vasculitis (inflammation of the blood vessels which can cause skin rashes, joint pain and kidney problems), neurological disorders such as encephalomyelitis (inflammation of the central nervous system), neuritis (inflammation of nerves) and a type of paralysis known as Guillain-Barré Syndrome.

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

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

5. HOW TO STORE FOCETRIA

Keep out of the reach and sight of children.

Do not use Focetria after the expiry date which is stated on the carton and the label. 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.

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 Focetria contains

- Active Substance:
  Influenza virus surface antigens (haemagglutinin and neuraminidase)* of strain:
  A/California/7/2009 (H1N1)v like strain (X-179A) 7.5 micrograms** per 0.5 ml dose

  * propagated in eggs
  ** expressed in microgram haemagglutinin.

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

- Adjuvant:
  The vaccine contains an 'adjuvant' (MF59C.1) to stimulate a better response. MF59C.1 is an oil/water emulsion containing 9.75 mg squalene, 1.175 mg polysorbate 80 and 1.175 mg sorbitan trioleate in a citrate buffer.

- Other Ingredients:
  The other ingredients are: thiomersal (multidose vial only), sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, sodium citrate, citric acid and water for injections.

What Focetria looks like and contents of the pack
Focetria is a milky-white liquid.
It is provided in:
- a ready-to-use syringe, containing a single dose (0.5 ml) for injection;
- vial containing ten doses (0.5 ml each) for injection.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Novartis Vaccines and Diagnostics S.r.l.
Via Fiorentina, 1 – Siena,
Italy.

Manufacturer

Novartis Vaccines and Diagnostics S.r.l.
Loc. Bellaria
53018 Rosia
Sovicille (SI)
Italy.

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

Instructions for mixing and administration of the vaccine:

Ready-to-use syringe, containing a single dose (0.5 ml) for injection:

The vaccine should be allowed to reach room temperature before use. Gently shake before use.

Vial containing ten doses (0.5 ml each) for injection:

Gently shake the multidose vial each time before withdrawing a dose (0.5 ml) of the vaccine into a syringe. Prior to administration, the withdrawn vaccine should be allowed reach room temperature.

The vaccine should not be administered intravascularly or subcutaneously.

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

This leaflet was last approved in 09/2009

Focetria has been authorised under "Exceptional Circumstances". The European Medicines Agency (EMEA) will regularly review any new information on the medicine and this package leaflet will be updated as necessary.

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