

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

## 1. NAME OF THE MEDICINAL PRODUCT

CELTURA suspension for injection in pre-filled syringe  
Pandemic H1N1 influenza vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

A/California/7/2009 (H1N1)v-like strain used (X-179A)                      3.75 micrograms\*\* per 0.25 ml dose

\* propagated in Madin Darby Canine Kidney (MDCK) cells

\*\* expressed in microgram haemagglutinin

Adjuvant MF59C.1 containing:

squalene	4.875 milligrams
polysorbate 80	0.588 milligrams
sorbitan trioleate	0.588 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.  
Pandemic influenza vaccine should be used in accordance with Official Guidance (see sections 4.2 and 5.1).

### 4.2 Posology and method of administration

The Clinical Particulars section will be updated in accordance with emerging additional data.

There is currently limited clinical experience with CELTURA (H1N1) in healthy adults, elderly, children or in adolescents (see section 5.1). The decision to use CELTURA (H1N1) in each age group defined below should take into account the extent of the clinical data available and the disease characteristics of the current influenza pandemic.

The dose recommendations are based on the:

- currently available immunogenicity and safety data obtained three weeks after administration of two doses of CELTURA (H1N1) to a limited number of healthy adults, including the elderly.
- currently available immunogenicity and safety data obtained three weeks after administration of a single dose of CELTURA (H1N1) to a limited number of healthy children and adolescent aged 12 months to 17 years.

See sections 4.8 and 5.1.

Posology:

Adults (18-50 years):

One dose of 0.25 ml at an elected date.

A second dose of vaccine should preferably be given. There should be an interval of at least three weeks between the first and second dose.

However, the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy adults aged 18-50 years suggest that a single dose may be sufficient in this age group.

Adults and Elderly (>50 years):

One dose of 0.25 ml at an elected date.

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

Children and adolescents aged 9-17 years:

One dose of 0.25 ml at an elected date.

A second dose of vaccine should preferably be given. There should be an interval of at least three weeks between the first and second dose.

However in selecting the dosing regimen, consideration may also be given to the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy adults.

Children and adolescents 6 months to 8 years of age:

One dose of 0.25 ml at an elected date.

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

In selecting the dosing regimen for children from 6 to 12 months of age, consideration may be given to the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy children aged 12 months to 8 years.

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.

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

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 of cetyltrimethylammonium bromide (CTAB) of this vaccine. However, in a pandemic situation, it may be appropriate to give the vaccine, provided that facilities for resuscitation are immediately available in case of need.

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

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

Caution is needed when administering this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients 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.

The vaccine should under no circumstances be administered intravascularly or subcutaneously.

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

#### **4.5 Interaction with other medicinal products and other forms of interaction**

There are no data on co-administration of CELTURA 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 results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique may disprove the false positive results and confirm the true results. The transient false positive reactions could be due to the IgM response by the vaccine.

#### **4.6 Pregnancy and lactation**

No data have been generated in pregnant women with CELTURA or with any other vaccine containing Adjuvant MF59C.1 (see section 5.3 Preclinical safety data).

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

The vaccine may be used during lactation.

#### **4.7 Effects on ability to drive and use machines**

CELTURA is unlikely to produce any effect on the ability to drive and use machines.

#### **4.8 Undesirable effects**

- Clinical trials

##### Adult and Elderly

In an ongoing clinical trial 185 adults aged 18-60 years and 135 elderly aged 61 years and older were exposed to at least one dose (3.75 µg HA H1N1 strain + MF59, in 0.25 mL) of the CELTURA pandemic vaccine. After the first and second vaccination, very commonly reported reactions in adults  $\geq 18$  years were: pain, erythema; fatigue, headache, myalgia, and sweating. Lower percentage of subjects reported these reactions after the second than after the first vaccination. Most of the reactions were mild in nature and of short duration. The incidence of symptoms observed in subjects over 60 years of age was generally lower as compared to the 18-60 year old population.

Adverse reactions from clinical trials with CELTURA are listed below.

Adverse reactions reported are listed according to the following frequency:

Very common ( $\geq 1/10$ ),

Common ( $\geq 1/100$  to  $< 1/10$ ),

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ),

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ ),

Very rare ( $< 1/10,000$ ).

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

#### Nervous system disorders

Very common: headache

Rare: convulsions

#### Skin and subcutaneous tissue disorders

Common: sweating

Rare: urticaria and eye swelling

#### Musculoskeletal, connective tissue and bone disorders

Very common: myalgia

Common: arthralgia

#### Gastrointestinal disorders

Common: nausea

#### General disorders and administration site conditions

Very common: injection site swelling, injection site pain, injection site induration, injection site redness, and fatigue

Common: injection site ecchymosis, fever, malaise and shivering

Rare: anaphylaxis

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

Limited preliminary data from clinical studies in children aged 9-17 years (N=165), 3-8 years (N=164) and 12-35 months (N=86), in which two different doses of Celtura H1N1 (3.75 µg with MF59 or 7.5 µg with MF59) were investigated, indicate that the side effect spectrum is similar to that observed in adults.

In another clinical study with the pandemic A/H5N1 strain of the CELTURA mock-up vaccine, the administration of two doses of 3.75 µg H5N1 + MF59 in 62 adults aged 18-40 years showed a comparable safety profile. Very commonly reported adverse reactions were pain, shivering, malaise, fatigue, headache, myalgia, arthralgia and sweating.

In clinical trials with different formulations (H5N3, H9N2 and H5N1) of the egg-derived vaccines authorised through mock-up procedure, approximately 3400 subjects were exposed. 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.

- Post-marketing surveillance

From Post-marketing surveillance with seasonal trivalent vaccines in all age groups and with the MF59 adjuvanted seasonal trivalent vaccine (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 (>1/1,000 to <1/100):

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

#### Rare (>1/10,000 to <1/1,000):

Neuralgia, paraesthesia, convulsions, transient thrombocytopenia.

Allergic reactions, in rare cases leading to shock, have been reported.

Very rare (<1/10,000):

Vasculitis with transient renal involvement and exudative erythema multiforme.

Neurological disorders, such as encephalomyelitis, neuritis and Guillain Barré syndrome.

Adverse event(s) from post-marketing surveillance with the pandemic vaccine: not applicable.

#### 4.9 Overdose

No case of overdose has been reported.

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC Code: J07BB02

Immunogenicity results for one or two doses of the 3.75µg CELTURA (H1N1) pandemic vaccine from the ongoing clinical trial for adults and elderly are shown below. The seroprotection rate\*, seroconversion rate\* and the seroconversion factor\*\* for anti-HA antibody in the adults measured by HI were as follows:

anti-HA antibody	Adults (18-60 years) N=183	Elderly (>60 years) N=135
Immune response 21 days after the first dose		
Seroprotection rate*	77% (95% CI: 70 - 83)	44% (95% CI: 35 - 53)
Seroconversion rate*	73% (95% CI: 66 - 79)	35% (95% CI: 27 - 43)
Seroconversion factor**	12 (95% CI: 9.4 - 15)	3.42 (95% CI: 2.78 - 4.4)
Immune response 21 days after the second dose		
Seroprotection rate	95% (95% CI: 91 - 98)	76% (95% CI: 68 - 83)
Seroconversion rate	93% (95% CI: 88 - 96)	69% (95% CI: 60 - 77)
Seroconversion factor	23 (95% CI: 19 - 28)	8.97 (95% CI: 7.14 - 11)

\* measured by HI assay, HI titer  $\geq 1:40$

\*\* geometric mean ratios of HI titer

A further post-hoc subgroup analysis of the available immunogenicity data showed a seroprotection rate of 63%, a seroconversion rate of 56% and a seroconversion factor of 7.84 measured by HI assay following the administration of one dose of the vaccine in patients 51-60 years of age. After the second dose the seroprotection rate was 100%, the seroconversion rate 97%, and the seroconversion factor was 19.

#### 5.2 Pharmacokinetic properties

Not applicable.

#### 5.3 Preclinical safety data

No preclinical studies were done with CELTURA. No local or systemic toxicity was identified in a toxicology study in rabbits with an A/H5N1 cell culture vaccine with MF59.

There are no reproductive and developmental toxicity data in animals with CELTURA. There were no effects on reproduction or development in studies with MF59 adjuvant alone (rats, rabbits), seasonal cell culture vaccine (rabbits) or an egg-derived A/H5N1 vaccine with MF59 (rabbits).

## **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**

6 months.

### **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**

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

### **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 GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
GERMANY

## **8. MARKETING AUTHORISATION NUMBER(S)**

PEI.H.11428.01.1

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

4. November 2009

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

October 2009

## 1. NAME OF THE MEDICINAL PRODUCT

CELTURA suspension for injection in multidose container  
Pandemic H1N1 influenza vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

A/California/7/2009 (H1N1)v-like strain used (X-179A) 3.75 micrograms\*\* per 0.25 ml dose

\* propagated in Madin Darby Canine Kidney (MDCK) cells

\*\* expressed in microgram haemagglutinin

Adjuvant MF59C.1 containing:

squalene	4.875 milligrams
polysorbate 80	0.588 milligrams
sorbitan trioleate	0.588 milligrams

Excipients:

thiomersal	0.025 milligrams
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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.

Milky-white liquid.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Prophylaxis of influenza in an officially declared pandemic situation.

Pandemic influenza vaccine should be used in accordance with Official Guidance (see sections 4.2 and 5.1).

### 4.2 Posology and method of administration

The Clinical Particulars section will be updated in accordance with emerging additional data.

There is currently limited clinical experience with CELTURA (H1N1) in healthy adults, elderly, children or in adolescents (see section 5.1). The decision to use CELTURA (H1N1) in each age group defined below should take into account the extent of the clinical data available and the disease characteristics of the current influenza pandemic.

The dose recommendations are based on the:

- currently available immunogenicity and safety data obtained three weeks after administration of two doses of CELTURA (H1N1) to a limited number of healthy adults, including the elderly.
- currently available immunogenicity and safety data obtained three weeks after administration of a single dose of CELTURA (H1N1) to a limited number of healthy children and adolescent aged 12 months to 17 years.

See sections 4.8 and 5.1.

Posology:

Adults (18-50 years):

One dose of 0.25 ml at an elected date.

A second dose of vaccine should preferably be given. There should be an interval of at least three weeks between the first and second dose.

However, the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy adults aged 18-50 years suggest that a single dose may be sufficient in this age group.

Adults and Elderly (>50 years):

One dose of 0.25 ml at an elected date.

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

Children and adolescents aged 9-17 years:

One dose of 0.25 ml at an elected date.

A second dose of vaccine should preferably be given. There should be an interval of at least three weeks between the first and second dose.

However in selecting the dosing regimen, consideration may also be given to the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy adults.

Children and adolescents 6 months to 8 years of age:

One dose of 0.25 ml at an elected date.

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

In selecting the dosing regimen for children from 6 to 12 months of age, consideration may be given to the currently available immunogenicity data obtained at three weeks after administration of CELTURA (H1N1) to a limited number of healthy children aged 12 months to 8 years.

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.

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

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 of cetyltrimethylammonium bromide (CTAB) of this vaccine. However, in a pandemic situation, it may be appropriate to give the vaccine, provided that facilities for resuscitation are immediately available in case of need.

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

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

Caution is needed when administering this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients, to thiomersal and to 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.

The vaccine should under no circumstances be administered intravascularly or subcutaneously.

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

#### **4.5 Interaction with other medicinal products and other forms of interaction**

There are no data on co-administration of CELTURA 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 results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique may disprove the false positive results and confirm the true results. The transient false positive reactions could be due to the IgM response by the vaccine.

#### **4.6 Pregnancy and lactation**

No data have been generated in pregnant women with CELTURA or with any other vaccine containing Adjuvant MF59C.1 (see section 5.3 Preclinical safety data).

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

The vaccine may be used during lactation.

#### **4.7 Effects on ability to drive and use machines**

CELTURA is unlikely to produce any effect on the ability to drive and use machines.

#### **4.8 Undesirable effects**

- Clinical trials

##### Adult and Elderly

In an ongoing clinical trial 185 adults aged 18-60 years and 135 elderly aged 61 years and older were exposed to at least one dose (3.75 µg HA H1N1 strain + MF59, in 0.25 mL) of the CELTURA pandemic vaccine. After the first and second vaccination, very commonly reported reactions in adults  $\geq 18$  years were: pain, erythema; fatigue, headache, myalgia, and sweating. Lower percentage of subjects reported these reactions after the second than after the first vaccination. Most of the reactions were mild in nature and of short duration. The incidence of symptoms observed in subjects over 60 years of age was generally lower as compared to the 18-60 year old population.

Adverse reactions from clinical trials with CELTURA are listed below.

Adverse reactions reported are listed according to the following frequency:

Very common ( $\geq 1/10$ ),

Common ( $\geq 1/100$  to  $< 1/10$ ),

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ),

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ ),  
Very rare ( $< 1/10,000$ ).

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

Nervous system disorders

Very common: headache  
Rare: convulsions

Skin and subcutaneous tissue disorders

Common: sweating  
Rare: urticaria and eye swelling

Musculoskeletal, connective tissue and bone disorders

Very common: myalgia  
Common: arthralgia

Gastrointestinal disorders

Common: nausea

General disorders and administration site conditions

Very common: injection site swelling, injection site pain, injection site induration, injection site redness, and fatigue  
Common: injection site ecchymosis, fever, malaise and shivering  
Rare: anaphylaxis

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

Limited preliminary data from clinical studies in children aged 9-17 years (N=165), 3-8 years (N=164) and 12-35 months (N=86), in which two different doses of Celtura H1N1 (3.75  $\mu\text{g}$  with MF59 or 7.5  $\mu\text{g}$  with MF59) were investigated, indicate that the side effect spectrum is similar to that observed in adults.

In another clinical study with the pandemic A/H5N1 strain of the CELTURA mock-up vaccine, the administration of two doses of 3.75  $\mu\text{g}$  H5N1 + MF59 in 62 adults aged 18-40 years showed a comparable safety profile. Very commonly reported adverse reactions were pain, shivering, malaise, fatigue, headache, myalgia, arthralgia and sweating.

In clinical trials with different formulations (H5N3, H9N2 and H5N1) of the egg-derived vaccines authorised through mock-up procedure, approximately 3400 subjects were exposed. 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.

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From Post-marketing surveillance with seasonal trivalent vaccines in all age groups and with the MF59 adjuvanted seasonal trivalent vaccine (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 ( $> 1/1,000$  to  $< 1/100$ ):

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

Rare (>1/10,000 to <1/1,000):

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

Very rare (<1/10,000):

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

Adverse event(s) from post-marketing surveillance with the pandemic vaccine: not applicable.

#### 4.9 Overdose

No case of overdose has been reported.

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC Code: J07BB02

Immunogenicity results for one or two doses of the 3.75µg CELTURA (H1N1) pandemic vaccine from the ongoing clinical trial for adults and elderly are shown below. The seroprotection rate\*, seroconversion rate\* and the seroconversion factor\*\* for anti-HA antibody in the adults measured by HI were as follows:

anti-HA antibody	Adults (18-60 years) N=183	Elderly (>60 years) N=135
Immune response 21 days after the first dose		
Seroprotection rate*	77% (95% CI: 70 - 83)	44% (95% CI: 35 - 53)
Seroconversion rate*	73% (95% CI: 66 - 79)	35% (95% CI: 27 - 43)
Seroconversion factor**	12 (95% CI: 9.4 - 15)	3.42 (95% CI: 2.78 - 4.4)
Immune response 21 days after the second dose		
Seroprotection rate	95% (95% CI: 91 - 98)	76% (95% CI: 68 - 83)
Seroconversion rate	93% (95% CI: 88 - 96)	69% (95% CI: 60 - 77)
Seroconversion factor	23 (95% CI: 19 - 28)	8.97 (95% CI: 7.14 - 11)

\* measured by HI assay, HI titer  $\geq 1:40$

\*\* geometric mean ratios of HI titer

A further post-hoc subgroup analysis of the available immunogenicity data showed a seroprotection rate of 63%, a seroconversion rate of 56% and a seroconversion factor of 7.84 measured by HI assay following the administration of one dose of the vaccine in patients 51-60 years of age. After the second dose the seroprotection rate was 100%, the seroconversion rate 97%, and the seroconversion factor was 19.

#### 5.2 Pharmacokinetic properties

Not applicable.

#### 5.3 Preclinical safety data

No preclinical studies were done with CELTURA. No local or systemic toxicity was identified in a toxicology study in rabbits with an A/H5N1 cell culture vaccine with MF59.

There are no reproductive and developmental toxicity data in animals with CELTURA. There were no effects on reproduction or development in studies with MF59 adjuvant alone (rats, rabbits), seasonal cell culture vaccine (rabbits) or an egg-derived A/H5N1 vaccine with MF59 (rabbits).

## **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**

6 months.

After withdrawal of the first dose, the vaccine should be used within 6 hours.

This recommendation is based on data derived from controlled experiments demonstrating chemical and physical stability as well as microbiological quality for 6 hours. From a microbiological point of view, minimisation of the risk of the contamination of the multidose vials during withdrawal of each dose is the responsibility of the user.

### **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 17-dose vials (type I glass) with stopper (halo-butyl rubber). Packs of 10.

### **6.6 Special precautions for disposal and other handling**

The vaccine should be allowed to reach room temperature before use. The volume of CELTURA (5 ml) corresponds to 17 vaccine doses. Before use the vial should be gently shaken. After shaking this results a milky-white liquid. In the event of variation being observed, discard the vaccine. Each vaccine dose of 0,25 ml is withdrawn into a syringe for injection. The needle used for withdrawal must be replaced by a needle suitable for injection.

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

## **7. MARKETING AUTHORISATION HOLDER**

Novartis Vaccines and Diagnostics GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
GERMANY

**8. MARKETING AUTHORISATION NUMBER(S)**

PEI.H.11428.01.1

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

4. November 2009

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

October 2009

## **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**

Manufacturer responsible for monovalent pooled harvest:

Novartis Vaccines and Diagnostics GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
Germany

Name and address of the manufacturer responsible for batch release

Novartis Vaccines and Diagnostics GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
Germany

**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.

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

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

Not applicable

• **OTHER CONDITIONS**

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

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

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

**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**

CELTURA suspension for injection in pre-filled syringe  
Pandemic H1N1 influenza vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

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

One dose (0.25 ml) contains: Active Ingredients: Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in MDCK cells\*, and adjuvanted with MF59C.1, of strain:

A/California/7/2009 (H1N1)v-like strain used (X-179A) 3.75 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.

\* Madin Darby Canine Kindey cells (MDCK)

**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.

10 x single dose (0.25 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 GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
Germany

**12. MARKETING AUTHORISATION NUMBER(S)**

PEI.H.11428.01.1

**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 17-DOSE VIAL**

#### **1. NAME OF THE MEDICINAL PRODUCT**

CELTURA suspension for injection in multidose container  
Pandemic H1N1 influenza vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

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

One dose (0.25 ml) contains: Active Ingredients: Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in MDCK cells\*, and adjuvanted with MF59C.1, of strain:

A/California/7/2009 (H1N1)v-like strain used (X-179A) 3.75 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.

\* Madin Darby Canine Kidney cells (MDCK)

#### **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 17 doses

1 dose (0.25 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 GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
Germany

**12. MARKETING AUTHORISATION NUMBER(S)**

PEI.H.11428.01.1

**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**

CELTURA  
Pandemic H1N1 influenza vaccine  
Intramuscular injection

**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**

1 dose (0,25 ml)

**6. OTHER**

Store in a refrigerator.

Novartis V&D GmbH & Co. KG

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**LABEL FOR 17-DOSE VIAL**

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

CELTURA  
Pandemic H1N1 influenza vaccine  
Intramuscular injection

**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 container (5 ml)

**6. OTHER**

Store in a refrigerator.

Novartis V&D GmbH & Co. KG

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### CELTURA suspension for injection in pre-filled syringe

Pandemic H1N1 Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

All information included in this package leaflet and in the labelling material accompanying this product has been printed in advance of its approval to facilitate the availability of the vaccine. For the most up-to-date information please consult the website of Paul-Ehrlich-Institut (PEI): <http://www.pei.de>

#### **Read all of this leaflet carefully before you start receiving this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- 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 CELTURA is and what it is used for
2. Before you receive CELTURA
3. How to receive CELTURA
4. Possible side effects
5. How to store CELTURA
6. Further information

### **1. WHAT CELTURA IS AND WHAT IT IS USED FOR**

Celtura is a vaccine used to prevent influenza (flu) in an officially declared pandemic.

Pandemic flu is a type of influenza that occurs every few decades and which spreads rapidly to affect most countries and regions around the world. The symptoms (signs) of pandemic flu are similar to those of an “ordinary” flu but are usually more severe.

The vaccine works by causing the body to produce its own protection (antibodies) against the disease. As with all vaccines, CELTURA may not fully protect all persons who are vaccinated.

### **2. BEFORE YOU RECEIVE CELTURA**

#### **Do not take CELTURA if you:**

- have experienced serious allergic reaction (i.e. life-threatening) to any of the constituents of CELTURA,
- are allergic (hypersensitive) to influenza vaccines or any of the ingredients of CELTURA,
- are allergic to cetyltrimethylammonium bromide (CTAB).

#### **Take special care with CELTURA if you:**

- feel feverish,
- have any illness or infection,
- are having immunosuppressive therapy, e.g. corticosteroid treatment or chemotherapy for cancer, or if you have any condition which makes you prone to infections (immunodeficiency conditions).

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

#### **Taking other medicines**

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines

obtained without a prescription. There is no data on administration of CELTURA at the same time with other vaccines. If another vaccine is required at the same time, then the injection should be carried out on a different limb. In such cases, the side effects may be more intense.

### **Pregnancy and breast-feeding**

There is no information on the use of CELTURA in pregnant women. Your doctor needs to assess the benefits and potential risks of giving you the vaccine if you are pregnant. Please tell your doctor if you are/may be pregnant or intend to become pregnant.

The vaccine may be used during lactation.

### **Driving and using machines**

The vaccine is unlikely to produce any effect on the ability to drive and use machines.

## **3. HOW TO RECEIVE CELTURA**

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 (18-50):

A dose (0.25 ml) of the vaccine will be given.

A second dose of 0.25 ml vaccine may be given after an interval of at least three weeks.

### Elderly (>50):

A dose (0.25 ml) of the vaccine will be given.

A second dose of 0.25 ml vaccine should be given after an interval of at least three weeks.

### Children and adolescents 9-17 years of age:

You or your child will receive one dose of 0.25 ml vaccine.

A second dose of 0.25 ml vaccine may be given after an interval of at least three weeks.

### Children 6 months to 8 years of age:

Your child will receive one dose of 0.25 ml vaccine and a second dose of 0.25 ml at least three weeks later.

### Children aged less than 6 months of age:

Vaccination is currently not recommended in this age group.

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

## **4. POSSIBLE SIDE EFFECTS**

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

### Common (in more than 1 out of 100 people, but less than 1 in 10).

Common side effects include: redness, swelling, or pain at the site of injection, and bruising or hardening of the skin at the injection site. In some cases the effects may also include raised temperature (fever), malaise (generally feeling unwell), shivering, tiredness, headache, sweating, pain in muscles and joints. These reactions usually disappear within 1-2 days without treatment. If they persist, CONSULT YOUR DOCTOR.

### Uncommon: (in more than 1 out of 1,000 people, but less than 1 in 100).

Uncommon side effects may include: generalised skin reactions including itching, bumps on the skin or a non-specific rash.

**Rare** (in more than 1 out of 10,000 people, but less than 1 in 1,000). Rare side effects include: neuralgia (pain along a nerve), numbness or tingling sensations, convulsions (fits) or transient thrombocytopenia (a low platelet count in the blood which can result in bleeding or bruising).

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.

**Very rare** (in less than 1 in 10,000). Very rare side effects include: vasculitis (inflammation of the blood vessels which can cause skin rashes, joint pain and kidney problems) and exudative Stevens-Johnson syndrome (erythema multiforme). 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 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 CELTURA

Keep out of the reach and sight of children.

Do not use CELTURA after the expiry date which is stated on the carton and the label after EXP. The expiry date refers to the last day of that month.

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

- **Active Substance:**  
CELTURA does not contain live virus particles and so it cannot cause Pandemic influenza. The active ingredients of the vaccine are purified viral proteins (called haemagglutinin and neuraminidase). They are isolated from the surface of influenza virus particles, which are grown in Madin Darby Canine Kidney (MDCK) cells (this is the special cell culture in which the influenza virus is grown). These viral proteins are prepared from the strain of influenza virus that complies with the WHO recommendations and EU decision in an officially declared Pandemic situation.  
One dose (0.25 ml) of the vaccine contains at least 3.75 micrograms of haemagglutinin from the following recommended influenza virus strain:  
  
A/California/7/2009 (H1N1)v-like strain used (X-179A)
- **Adjuvant:**  
The vaccine contains an 'adjuvant' (a compound containing squalene) to stimulate a better response. The adjuvant includes also polysorbate 80 and sorbitan trioleate in a citrate buffer.
- **Other Ingredients:**  
The other ingredients are: 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 CELTURA looks like and contents of the pack

CELTURA is a milky-white liquid.

It is provided in:

- ready-to-use syringe, containing a single dose (0.25 ml) for injection.

**Marketing Authorisation Holder and Manufacturer**  
Novartis Vaccines and Diagnostics GmbH & Co. KG  
Emil-von-Behring-Strasse 76  
D-35041 Marburg  
GERMANY

**This leaflet was approved in 10/2009.**

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### CELTURA suspension for injection in multidose container

Pandemic H1N1 Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures, adjuvanted)

All information included in this package leaflet and in the labelling material accompanying this product has been printed in advance of its approval to facilitate the availability of the vaccine. For the most up-to-date information please consult the website of Paul-Ehrlich-Institut (PEI): <http://www.pei.de>

#### **Read all of this leaflet carefully before you start receiving this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- 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 CELTURA is and what it is used for
2. Before you receive CELTURA
3. How to receive CELTURA
4. Possible side effects
5. How to store CELTURA
6. Further information

### **1. WHAT CELTURA IS AND WHAT IT IS USED FOR**

CELTURA is a vaccine used to prevent influenza (flu) in an officially declared pandemic.

Pandemic flu is a type of influenza that occurs every few decades and which spreads rapidly to affect most countries and regions around the world. The symptoms (signs) of pandemic flu are similar to those of an “ordinary” flu but are usually more severe.

The vaccine works by causing the body to produce its own protection (antibodies) against the disease. As with all vaccines, CELTURA may not fully protect all persons who are vaccinated.

### **2. BEFORE YOU RECEIVE CELTURA**

#### **Do not take CELTURA if you:**

- have experienced serious allergic reaction (i.e. life-threatening) to any of the constituents of CELTURA,
- are allergic (hypersensitive) to influenza vaccines or any of the ingredients of CELTURA,
- are allergic to cetyltrimethylammonium bromide (CTAB).

#### **Take special care with CELTURA if you:**

- feel feverish,
- have any illness or infection,
- are having immunosuppressive therapy, e.g. corticosteroid treatment or chemotherapy for cancer, or if you have any condition which makes you prone to infections (immunodeficiency conditions),

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

#### **Taking other medicines**

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. There is no data on administration of CELTURA at the same time with other vaccines. If another vaccine is required at the same time, then the injection should be carried out on a different limb. In such cases, the side effects may be more intense.

### **Pregnancy and breast-feeding**

There is no information on the use of CELTURA in pregnant women. Your doctor needs to assess the benefits and potential risks of giving you the vaccine if you are pregnant. Please tell your doctor if you are/may be pregnant or intend to become pregnant.

The vaccine may be used during lactation.

### **Driving and using machines**

The vaccine is unlikely to produce any effect on the ability to drive and use machines.

### **Important information about some of the ingredients of CELTURA**

This medicinal product in multidose 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.

## **3. HOW TO RECEIVE CELTURA**

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 (18-50):

A dose (0.25 ml) of the vaccine will be given.

A second dose of 0.25 ml vaccine may be given after an interval of at least three weeks.

### Elderly (>50):

A dose (0.25 ml) of the vaccine will be given.

A second dose of 0.25 ml vaccine should be given after an interval of at least three weeks.

### Children and adolescents 9-17 years of age:

You or your child will receive one dose of 0.25 ml vaccine.

A second dose of 0.25 ml vaccine may be given after an interval of at least three weeks.

### Children 6 months to 8 years of age:

Your child will receive one dose of 0.25 ml vaccine and a second dose of 0.25 ml at least three weeks later.

### Children aged less than 6 months of age:

Vaccination is currently not recommended in this age group.

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

## **4. POSSIBLE SIDE EFFECTS**

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

### Common (in more than 1 out of 100 people, but less than 1 in 10).

Common side effects include: redness, swelling, or pain at the site of injection, and bruising or hardening of the skin at the injection site. In some cases the effects may also include raised temperature (fever), malaise (generally feeling unwell), shivering, tiredness, headache, sweating, pain in muscles and joints. These reactions usually disappear within 1-2 days without treatment. If they persist, CONSULT YOUR DOCTOR.

Uncommon: (in more than 1 out of 1,000 people, but less than 1 in 100).

Uncommon side effects may include: generalised skin reactions including itching, bumps on the skin or a non-specific rash.

Rare (in more than 1 out of 10,000 people, but less than 1 in 1,000). Rare side effects include: neuralgia (pain along a nerve), numbness or tingling sensations, convulsions (fits) or transient thrombocytopenia (a low platelet count in the blood which can result in bleeding or bruising).

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.

Very rare (in less than 1 in 10,000). Very rare side effects include: vasculitis (inflammation of the blood vessels which can cause skin rashes, joint pain and kidney problems) and exudative Stevens-Johnson syndrome (erythema multiforme). 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 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 CELTURA

Keep out of the reach and sight of children.

Do not use CELTURA after the expiry date which is stated on the carton and the label after EXP. The expiry date refers to the last day of that month.

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

#### - Active Substance:

CELTURA does not contain live virus particles and so it cannot cause Pandemic influenza. The active ingredients of the vaccine are purified viral proteins (called haemagglutinin and neuraminidase). They are isolated from the surface of influenza virus particles, which are grown in Madin Darby Canine Kidney (MDCK) cells (this is the special cell culture in which the influenza virus is grown). These viral proteins are prepared from the strain of influenza virus that complies with the WHO recommendations and EU decision in an officially declared Pandemic situation.

One dose (0.25 ml) of the vaccine contains at least 3.75 micrograms of haemagglutinin from the following recommended influenza virus strain:

A/California/7/2009 (H1N1)v-like strain used (X-179A)

#### - Adjuvant:

The vaccine contains an 'adjuvant' (a compound containing squalene) to stimulate a better response. The adjuvant includes also polysorbate 80 and sorbitan trioleate in a citrate buffer.

#### - Other Ingredients:

The other ingredients are: sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, sodium citrate, citric acid, thiomersal and water for injections.

**What CELTURA looks like and contents of the pack**

CELTURA is a milky-white liquid.

It is provided in:

- vials containing seventeen doses (0.25 ml each) for injection.

**Marketing Authorisation Holder and Manufacturer**

Novartis Vaccines and Diagnostics GmbH & Co. KG

Emil-von-Behring-Strasse 76

D-35041 Marburg

GERMANY

**This leaflet was approved in 10/2009.**

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

The vaccine should be allowed to reach room temperature before use. The volume of CELTURA (5 ml) corresponds to 17 vaccine doses. Before use the vial should be gently shaken. Shaking results in a milky-white liquid. In the event of variation being observed, discard the vaccine. Each vaccine dose of 0.25 ml is withdrawn into a syringe for injection. The needle used for withdrawal must be replaced by a needle suitable for injection.